The Journal of Pediatrics

VOL. 12 FEBRUARY, 1938 No. 2

Original Communications

INCLUSION BLENNORRHEA

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INCLUSION blennorrhea is a chronic, nonbacterial form of conjunctivitis occurring in the neonatal period, and is thought to be due to the activity of a specific filterable virus. It is not a new disease but has received increasing recognition through recent researches concerning its etiology. It comprises about 10 to 20 per cent of the cases of ophthalmia neonatorum seen in hospitals, where gonorrheal ophthalmia is becoming a rarity. Published reports have been confined to the ophthalmologic periodicals; thus it would seem desirable to bring this entity to the attention of pediatrists, among whom it frequently goes unrecognized.

HISTORICAL

Morax[1] in 1903 recognized a benign form of purulent ophthalmia in the newborn, unassociated with any pathogenic bacteria. He thought the conjunctival inflammation, like "snuffles," might be a manifestation of hereditary syphilis. Later, in 1909, Heymann[2] discovered epithelial inclusions, similar to those found in trachoma, in stained smears of the conjunctival secretions of these cases. Morax, Lindner, and Bollack[3] in 1911 confirmed this work, but were unable to determine the origin of the inclusions. The name "Einschlussblennorrhöe" or Inclusion Blennorrhea was applied to the condition by Lindner.[4]

Since this initial work, many theories have been propounded concerning the etiology of the inclusions. Lindner considered them to be intracellular groups of the causal organism. Stewart[5] concluded that inclusion blennorrhea was not a separate entity, but merely gonorrheal

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ophthalmia, and stated that the inclusions were only clumps of phagocytosed gonococci. Lumbroso[6] considered the inclusions to be reaction products of the cells to a filterable virus. The work of McKee[7] had led him to the belief that the inclusions are formed by phagocytosis of bacteria which are not the cause of the disease, but which may carry the virus. Thygeson[8] has reported a series of experimental studies which

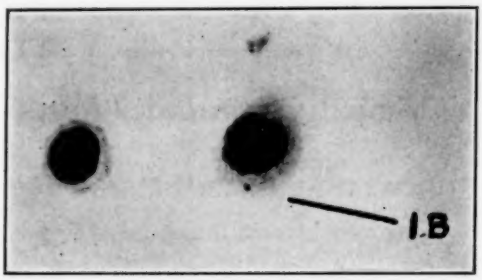

Fig. 1.—*I.B.*, initial body contained in the cytoplasm of an epithelial cell (×970).

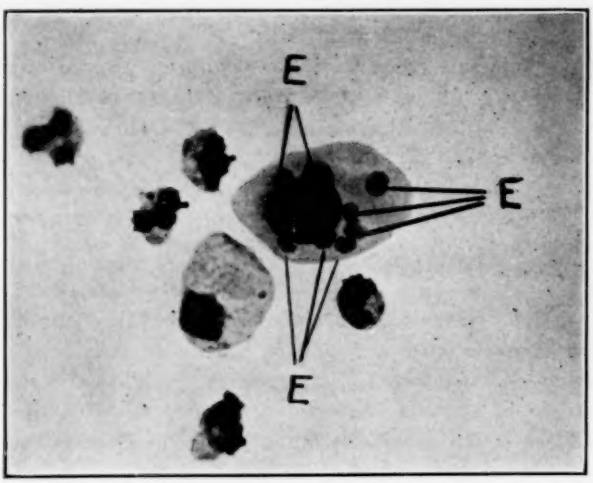

Fig. 2.—*E*, numerous clusters of elementary bodies contained within the cytoplasm of a single epithelial cell (×970).

lead him to conclude that the cytoplasmic inclusion bodies constitute intracellular colonies of a specific filterable virus in various stages of development.

ETIOLOGY

Thygeson believes the etiologic agent of the disease is a filterable virus having an elementary body phase and an initial body phase. In preparations of the secretion from acute cases of inclusion blennorrhea

stained by a modification* of the Giemsa technique, both phases may be found included in the leucocytes and epithelial cells. The elementary bodies may also be found extracellularly. The initial bodies are coccobacillary in shape, ranging from 0.3 to 0.8 microns in greatest diameter. They stain blue and usually more intensely at the poles. The elementary bodies are smaller, sharply defined granules, averaging 0.25 microns in diameter, occurring singly and in clusters of varying size. They stain reddish blue. All forms of the inclusion bodies may be found in an ordinary Giemsa-stained smear of the conjunctival secretions, but are much more readily identified in preparations of epithelial scrapings from the conjunctiva. Both initial and elementary bodies show up well

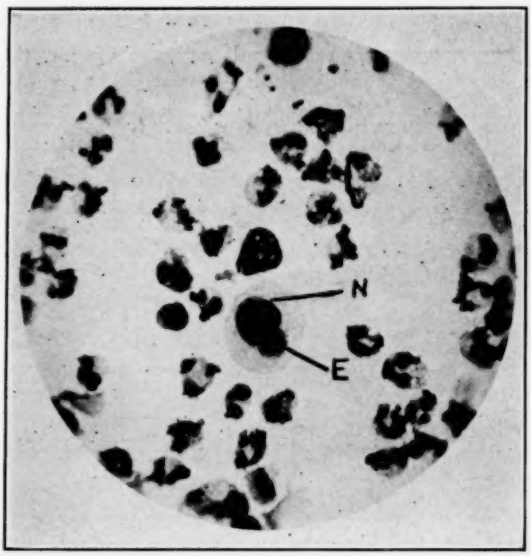

Fig. 3.—*N*, nucleus of epithelial cell. *E*, single cluster of elementary bodies indenting the nucleus, but without destruction of the nuclear membrane (×970).

in the pale staining cytoplasm of epithelial cells. The intracellular clusters are quite typical in appearance, but the free forms, even when numerous, are more difficult to identify.

The etiologic significance of these bodies was indicated by a carefully controlled series of experiments performed by Thygeson, the results of which he summarized as follows:

1. Constant presence of the inclusions in the disease.
2. Absence of inclusions in conjunctivitis of known bacterial origin.

*The usual technique for the Giemsa stain is followed. The slide is kept in the solution approximately twenty minutes, in a perpendicular position to prevent precipitation. The slide is removed, washed with water, then passed through two washes of five seconds each in 95 per cent alcohol. This serves to decolorize the acidophilic and neutrophilic granules in the cells, thus making the inclusion bodies, which are alcohol fast, stand out more clearly.

3. Absence of pathogenic bacteria in inclusion blennorrhea, and the failure of occasional saprophytes present to produce the disease when used for inoculation.

4. Multiplication of the elementary and initial bodies in the new host when the disease is transferred to the normal human conjunctiva.

5. Production of the disease with bacteria-free suspensions of elementary bodies.

6. Filtrates not containing elementary bodies are not infective.

Observations made from experimental transmission of the infection have led Thygeson to postulate the existence of a forty-eight-hour life cycle for the virus. As observed in the experimentally inoculated susceptible host, the transition from the elementary body phase, through the

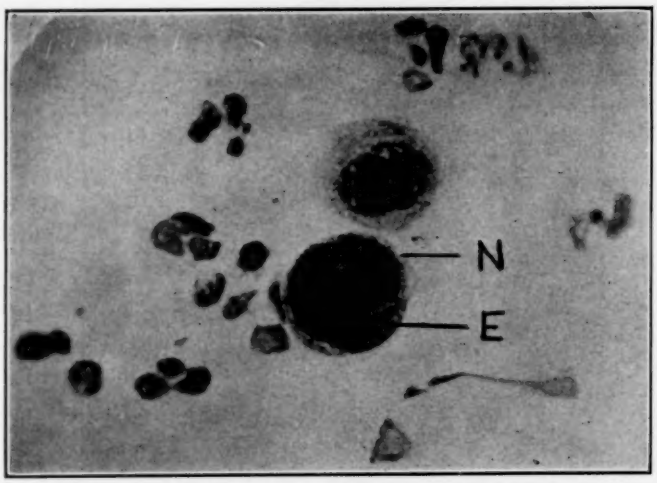

Fig. 4.—*E*, large cluster of elementary bodies, practically filling the epithelial cell. *N*, nucleus, compressed and partially destroyed by the growing virus colony (×970).

various forms of the virus, to the development of new elementary bodies, requires approximately forty-eight hours. From the examination of smears made at regular intervals during this period, the various stages of development of the virus may be accurately determined. The elementary body enters a cell and finding suitable nutrient material, develops into an initial body. This in turn divides and forms the mulberry mass or cluster of new elementary bodies, this large inclusion body usually capping the nucleus. The nuclear membrane then becomes weakened, ruptures, and the elementary bodies fill the entire cell. Due to internal pressure or external trauma, the cell then ruptures with discharge of the elementary bodies. These may then take up their abode in new cells. This explanation agrees closely with the observations of Bedson on the life cycle of the virus of spittacosis.

Opinion, however, is not unanimous concerning the etiology of this condition. McKee,[7] in his study of 27 cases of purulent ophthalmia in the newborn, found epithelial cell inclusions alone in 8 cases, while in as many more instances the inclusions were found associated with the gonococcus. In one instance inclusions were present in a streptococcic conjunctivitis. As previously mentioned, McKee believes that the inclusions are made up of phagocytosed bacteria. The apparent occurrence of cases of pure inclusion body conjunctivitis is explained as being due to the admitted difficulty in proving the presence of organisms in all cases. He later states, in referring to the inclusions of trachoma, swimming bath conjunctivitis, and inclusion blennorrhea, that while the inclusions are undoubtedly due to phagocytosed bacteria, these bacteria may not be the cause of the disease, but may carry the virus if such is the causal agent.

Clapp, in discussing a report by Thygeson and Mengert[9] on the properties of the virus of inclusion blennorrhea, states his belief that the inclusion bodies probably represent a cellular reaction rather than a stage in the development of the virus.

Thygeson believes that the epidemic form of swimming bath conjunctivitis represents the adult infection with the virus of inclusion blennorrhea.

Gifford and Lazar[10] tried to produce inclusions in the conjunctival epithelium of newborn infants by the application of a 2 per cent infusion of senega. Three of the 26 infants developed inclusions. Repeating this work on a series of 27 infants, they were unable to duplicate their findings. As a result of their experiences they assumed that the virus of inclusion blennorrhea was present in a latent form, and activated by the presence of a chemical irritant.

While Thygeson's work has not been completely accepted, a more satisfactory explanation of the etiology of inclusion blennorrhea has not been offered.

During the six months from January 1 to July 1, 1937, 30 cases of purulent ophthalmia in the newborn were observed on the obstetric and pediatric services of the Strong Memorial and Rochester Municipal Hospitals. Cultures and smears were made in each instance to determine the etiology, in an attempt to confirm the bacteriologic findings of Thygeson.

All inoculations were made on Bradford's* medium, which was found to be an excellent culture material for all the conjunctival organisms, pathogenic and nonpathogenic, including the gonococcus. In all doubt-

*Bradford's medium is made using 100 c.c. of 2 per cent Douglas agar of pH 7.6 to 7.8, to which has been added 25 c.c. of sterile ascitic or hydrocele fluid, 5 c.c. of a sterile 20 per cent solution of glucose, and 10 c.c. of sterile defibrinated rabbit's blood. The mixture is poured into sterile Petri dishes.

ful cases, special gonococcus cultures were made on chocolate agar plates and incubated in sealed glass jars containing 8 to 10 per cent of carbon dioxide.

TABLE I

ORGANISM	NUMBER OF CASES	NUMBER OF CASES CONTAINING INCLUSIONS
Hemolytic staphylococcus	15	0
H. influenza	3	0
D. pneumoniae	2	0
Hemolytic para-influenza	1	0
Streptococcus hemolyticus	1	0
Nonpathogens (diphtheroids and nonhemolytic staphylococci)	3	3
No organisms isolated	5	4
Totals	30	7

Of the 30 infants examined, a bacteriologic diagnosis was possible in 22. In none of these were inclusions found in the Giemsa-stained smears. Intracellular groups of organisms were frequently seen in the bacterial cases but they in no way resembled true inclusion bodies as found in the nonbacterial cases. In 8 infants cultures were either sterile or grew only the nonpathogenic diphtheroids and nonhemolytic staphylococci. Seven of these 8 cases showed typical cytoplasmic inclusions in successive preparations of conjunctival secretions stained by the Giemsa method. In the eighth case, no etiologic agent was determined. This may represent a failure to isolate the causal organism, or the inclusions may have been missed. No case of gonorrheal ophthalmia was seen.

These bacteriologic findings tend to substantiate Thygeson's statements that true cytoplasmic inclusions do not occur in conjunctivitis of known bacterial origin, and that pathogenic bacteria are not found in inclusion blennorrhea.

PATHOLOGY

Thygeson[8] has reported the examination of tissue sections in one case of inclusion blennorrhea. The sections were taken through the upper fornix, and revealed a dense subepithelial infiltration with all types of inflammatory cells, chiefly plasma cells. No follicle formation was noted, though it has been seen in experimental infections in adults and in the baboon. The epithelium was infiltrated with polymorphonuclear leucocytes, and in the superficial layers an occasional cytoplasmic inclusion body was seen.

EPIDEMIOLOGY

The fact that inclusion blennorrhea characteristically occurs in the newborn infant naturally led to the suspicion that it was transmitted during passage through the birth canal, as in the case of gonorrheal ophthalmia. Vaginal discharge has been a frequent finding in the mothers of these infants. Examination of cervical smears stained by

the Giemsa method has shown the presence of typical inclusions in the epithelial cells. Thygeson and Mengert[9] found inclusions in the cervical epithelium of 7 of 9 mothers of infants with inclusion blennorrhea. They also report an instance in which a gynecologist became infected accidentally during the performance of a dilatation and curettage. This infection ran a course typical of inclusion blennorrhea in the adult. The patient upon whom the operation was performed was examined three months later but at that time no inclusions could be demonstrated in cervical smears.

These investigators also searched for evidences of an inclusion infection in the urethras of male patients. In 11 cases of nonspecific urethritis, inclusions were found in one instance. The urethritis in this case healed after a duration of seven months.

In the present series of cases cervical smears were obtained from only one mother. Diligent search revealed 2 or 3 cells appearing to contain initial bodies. Other slides were not available to make more certain of their presence.

Transmission from one infant to another has not been observed; however, in the obstetric nursery it is the custom to isolate all cases of purulent ophthalmia when first observed. In one instance in this series, inclusion conjunctivitis occurred in one of a pair of twins. At the end of five months, the conjunctivitis was still active, while the other twin remained completely free of the disease.

There is no permanent local immunity since reinfection can be readily obtained in the experimental transmission of the disease to baboons. The virus confers no general immunity as shown by the lack of neutralizing antibodies or agglutinins for the elementary bodies in the blood of infected individuals.

CLINICAL FEATURES

The incubation period appears to be between five and ten days. As a rule, the onset of symptoms is usually between the seventh and tenth days of life. At first there may be only moderate reddening of the conjunctiva with the appearance of a small amount of purulent secretion at the inner canthus of the eye. It may be unilateral at the onset but always spreads to involve the other eye. Many cases remain relatively mild, the inflammation involving chiefly the conjunctiva of the lower tarsal plate.

In the more severe cases the condition takes on the appearance of an acute ophthalmia, with swelling and redness of the eyelids, intense, beefy redness of the palpebral conjunctiva, injection of the bulbar conjunctiva, and a profuse purulent discharge. The palpebral fissures are tightly closed. There is occasionally noted a tendency to the formation of a pseudomembrane on the conjunctiva. Clinically it may be impossible to differentiate this condition from a gonorrheal ophthalmia.

True follicles are not seen, but a papillary conjunctivitis is common. Corneal ulceration does not occur in neonatal inclusion blennorrhea, nor are there any vascular changes at the limbus such as are found in trachoma.

In spite of the frequent severity of local manifestations, systemic reactions have not been observed in these infants, nor has there been any evidence of spread of the infection to the other orbital structures.

COURSE AND PROGNOSIS

Under appropriate management the acute manifestations usually subside in a few days. The eyes lose their swollen reddened appearance and the discharge lessens considerably, but the beefy redness of the conjunctiva may persist for weeks. During this period the inclusions are still present, their numbers decreasing as the eyes improve. For months there may persist a moderate injection of the conjunctiva with a small amount of purulent material collecting at the inner canthi and along the lid margins. The inclusions become increasingly more difficult to find, and it has been noted that mild symptoms may persist after the smears have been repeatedly negative.

There are no recognizable complications or sequelae in inclusion blennorrhea, and after a period which may last several months, all signs disappear. None of the cases reported here have been observed for a sufficient length of time to make definite statements in this regard, but all are progressing satisfactorily after periods of activity ranging from two to six months.

DIAGNOSIS

Diagnosis can only be established definitely by the discovery of typical inclusions in Giemsa-stained preparations of the conjunctival secretion. Cultures from cases of inclusion blennorrhea are either sterile, or show only those bacteria which are known to be nonpathogenic to the conjunctiva, namely, diphtheroids and nonhemolytic staphylococci. An exception to this statement occurs in an occasional case in which a double infection or secondary infection is found. In such instances, both inclusions and a pathogenic bacterium may be found. Appropriate treatment will eliminate the latter, while the inclusion blennorrhea persists and follows its usual chronic course.

In any case of purulent ophthalmia, inclusion blennorrhea may be suspected when repeated cultures and smears have failed to show any pathogenic organisms. The mild irritative chemical conjunctivitis occurring during the first two or three days of life should cause little difficulty in differential diagnosis. Differentiation from gonorrheal ophthalmia or from a purulent ophthalmia due to one of the usual conjunctival pathogens is almost impossible from symptoms alone. Re-

peated smears and cultures of the conjunctival secretions, and the use of the Giemsa stain will make an accurate diagnosis possible in the majority of cases of ophthalmia neonatorum.

TREATMENT

Because all forms of the so-called ophthalmia neonatorum are similar in appearance, the usual treatment for gonorrheal ophthalmia is instituted when symptoms first present themselves. Whenever the diagnosis of inclusion blennorrhea is made, therapy should be modified somewhat. All the common ophthalmic antiseptics, both liquids and ointments, have been shown to have no influence on the course of this disease; on the contrary, one will occasionally find that symptoms are aggravated by too active treatment.

In the absence of any known specific therapeutic agent, treatment should be directed at symptomatic relief of the acute manifestations and prevention of secondary infection. With this in mind the following form of management is suggested. In the acute stage cold boric compresses are applied to the eyes for a few minutes every two or three hours. After compressing, the eyes are gently irrigated with boric acid solution, using a rubber ear syringe. Irrigations are followed 2 or 3 times daily by the instillation of 2 drops of 1 per cent mercurochrome (aqueous solution) into the conjunctival sac of each eye. This treatment is continued for the duration of the acute symptoms.

When swelling and redness of the lids have diminished or disappeared and the discharge has lessened, compressing is discontinued. Boric acid irrigations are continued 2 or 3 times daily, followed by the instillation of mercurochrome. When the infant is discharged from the hospital, the mother is instructed in the manner of giving irrigations, and is told to continue them as long as signs persist. Mercurochrome is also best continued at home, at least for a short period.

After six or eight weeks of this regime, the eyes appear almost normal to casual inspection. Examination will reveal a moderate injection of the conjunctiva, with the collection of a small amount of exudate at the inner canthi and along the lid margins. In this stage, the disease then persists until its course is run.

Probably the mechanical cleansing with boric acid is the most important factor in caring for this condition. Mercurochrome serves to prevent secondary infection, although other mild antiseptic solutions will serve the same purpose. There seems to be no indication for the application of silver nitrate to the lids; rather, one should seek to avoid all trauma to the conjunctiva. The danger of argyria should always be remembered in the long continued use of silver preparations.

In those cases beginning unilaterally, one may expect the opposite eye to become affected within a few days. The severity of involvement of the other eye may be greatly lessened by using the irrigations and instillations in both eyes.

SUMMARY

Recent researches indicate that inclusion blennorrhea is a specific, nonbacterial form of conjunctivitis due to the activity of a filterable virus. It is apparently transmitted to the infant from the mother during passage through the birth canal. It appears from the fifth to the tenth day of life, and its course, while self-limited, may extend over a period of many months. Diagnosis can only be established by means of examination of Giemsa-stained preparations of the conjunctival secretions. Cultures are either sterile or show only the usual nonpathogenic conjunctival organisms. In the absence of a specific therapeutic agent, treatment should be symptomatic, with the prevention of secondary infection.

Bacteriologic studies should be made a part of the routine in examining every case of ophthalmia neonatorum, however mild, and each examination should include a study of the exudate and conjunctival scrapings after special staining by the Giemsa method.

CASE REPORTS

CASE 1.—S. A., a boy, Unit No. 124109, was born Jan. 8, 1937, at another hospital in the city, Credé prophylaxis being used. On January 17, the tenth day of life, the infant developed a bilateral purulent conjunctivitis, so severe that both eyes were swollen completely shut. The mother had a vaginal discharge prior to delivery, but gonococci could not be identified by smear or culture. Cultures of the eye discharge failed to reveal gonococci. Treatment with boric acid and argyrol failed to result in improvement, and the infant was referred to this hospital for treatment.

Examination on January 31 showed both eyes to be swollen completely shut, with marked edema and redness. There was a bilateral beefy red papillary conjunctivitis, and the bulbar conjunctiva of the right eye was injected. The corneas were normal. The discharge was quite profuse, but thicker from the right eye than the left. Four successive cultures and smears failed to reveal the presence of gonococci. Four cultures on Bradford's medium failed to show any growth. Smears by Gram's method showed no organisms. Giemsa-stained preparations showed the presence of a moderate number of cytoplasmic inclusions and free elementary bodies in both eyes.

Treatment was begun with cold compresses, boric acid irrigations and mercurochrome. The acute phase subsided in four days, but the beefy red appearance of the conjunctiva persisted for several weeks. This child has been examined at monthly intervals. The secretions have gradually diminished and, at the last examination, there was only a moderate conjunctivitis, without noticeable discharge. Inclusions could be demonstrated for four months, but at the last examination none were found.

CASE 2.—C. A. B., a girl, Unit No. 123724, one of female twins, was born in this hospital Jan. 19, 1937, Credé prophylaxis being employed. A mild conjunctivitis was noted on January 28, involving only the left eye. There was a small amount of purulent exudate present. Cultures and smears were made which showed the presence of nonhemolytic staphylococci and diphtheroids. Giemsa staining showed a large number of typical cytoplasmic inclusions.

The infant was seen in the pediatric out-patient department on February 11, at which time the right eye had become involved in a similar manner. Both eyes

were sealed shut with a gummy secretion. The conjunctivae were moderately reddened. Bacteriologic studies again showed diphtheroids and nonhemolytic staphylococci, while cytoplasmic inclusions were numerous in the secretions from both eyes.

Treatment was begun with boric acid and mercurochrome. Cultures on three subsequent occasions were sterile, while inclusion bodies continued to be numerous. At the last examination, the conjunctivitis had dwindled to a small collection of secretion at the inner canthi, and a mild redness of the conjunctivae. Inclusions were not found at the last examination five months after the onset. This infant is now developing the physical characteristics of mongolism. The twin is entirely normal and has not shown any signs of conjunctivitis.

CASE 3.—P. E., a girl, Unit No. 125653, was born at home on March 10, 1937, Credé prophylaxis being used. On March 18 there developed a profuse purulent discharge from the right eye. The left eye became involved the following day. The lids were red and edematous, and the palpebral fissures crusted and closed. The conjunctivae were beefy red. The corneas were normal. The child was referred to the hospital for diagnosis and treatment.

The infant's Wassermann and Kahn tests were negative.

Four cultures and smears failed to show any gonococci. In each instance diphtheroids and nonhemolytic staphylococci were isolated. Inclusions were numerous in Giemsa-stained preparations of material from both eyes. Subsequent examination during the next three months showed a gradual diminution of signs under treatment. Cultures were negative, but inclusions were still present in small numbers, at the last examination on June 3.

CASE 4.—C., a girl, Unit No. 125842, was born in this hospital on March 20, 1937, Credé prophylaxis being used. She was first noticed to have a conjunctivitis on March 26. The left eye was involved first, followed in two days by a similar involvement of the right eye. Examination on March 29 showed slight edema and redness of the external ocular tissues, with inflammation of the palpebral conjunctivae. A small amount of purulent discharge was present. The corneas were normal.

Two successive cultures were sterile. Smears stained by Gram's method showed no organisms. A moderate number of inclusions were demonstrated in Giemsa-stained preparations.

The mother had a mild vaginal discharge before delivery. Repeated cervical smears were made after a diagnosis had been established in the infant, but careful examination showed suggestive inclusions in only one smear. The cytoplasmic inclusions were not typical, but because of the large number of bacteria present, it was impossible to say whether these were true inclusions. The mother's Wassermann was negative.

This infant has not been seen since the initial examination.

CASE 5.—R. J. H., a boy, Unit No. 126239, was born in this hospital on April 1, 1937, Credé prophylaxis being used. On April 7 the left eye was noted to be swollen shut with a profuse thick yellow secretion pouring from the palpebral fissure. The right eye showed a mildly reddened conjunctiva. Cultures and smears from both eyes failed to reveal any organisms. No organisms were seen in smears stained by Gram's method, but with the Giemsa stain, a moderate number of cytoplasmic inclusions were found in material from the left eye. Treatment was begun with cold compresses to the left eye and boric acid irrigations and mercurochrome instillations applied to both eyes. The left eye subsided rather promptly and the child was sent home, using boric acid and zinc sulphate solution.

The child was seen in the pediatric out-patient department on April 29, at which time there was a moderate purulent exudate from both eyes. Cultures were negative,

while inclusions were found in secretions from both eyes. When last examined on May 20, there was still a mild conjunctivitis, and inclusions could be demonstrated in small numbers.

CASE 6.—J. A. B., a girl, Unit No. 126807, was born in another hospital on April 12, 1937, with Credé prophylaxis being used. The eyelids were slightly swollen and discolored at birth, which was explained as being due to a difficult delivery. On April 18 the infant developed a profuse purulent discharge from both eyes. There was no history of a vaginal discharge in the mother. The child was referred to this hospital for treatment.

Examination on April 20 showed marked edema and redness of the lids of both eyes. The palpebral fissures were sealed shut. As soon as they were opened a thick creamy exudate appeared. The palpebral conjunctivae were beefy red, and the bulbar conjunctivae injected. The corneas were normal.

Three cultures and smears were negative for the gonococcus. Diphtheroids and a nonhemolytic staphylococcus were isolated from the left eye. A large number of inclusions were found in preparations from both eyes.

Compresses, boric acid irrigations, and mercurochrome were used, and at the time of discharge from the hospital on May 8, all that remained was a beefy redness of the conjunctivae. Inclusions were still numerous. This case was referred by a private physician, and was not seen again.

CASE 7.—A. M. A., a girl, Unit No. 126432, was born in this hospital on April 12, 1937. The Credé prophylaxis was used. On April 21, the tenth day of life, a purulent discharge from the left eye was noted. The lids were swollen shut. The right eye was normal except for redness of the conjunctiva. The mother gave no history of vaginal discharge and her Wassermann and Kahn tests were negative.

Examination on April 30 showed a slight purulent discharge from the right eye, with redness of the conjunctiva. The left eye was swollen shut, and a profuse creamy discharge appeared between the lid margins. There was a beefy red papillary conjunctivitis. The cornea was normal. Two cultures were negative at the end of seventy-two hours. Preparations of the conjunctival secretion stained by Gram's method failed to show any organisms. Giemsa-stained preparations from both eyes showed many cytoplasmic inclusions characteristic of inclusion blennorrhea.

Treatment was carried out at home, and consisted of 3 per cent boric acid irrigations and instillation of 1 per cent mercurochrome. There was prompt relief of the acute symptoms. Three subsequent examinations again showed negative cultures with cytoplasmic inclusions demonstrated in Giemsa-stained preparations in each instance. The last examination on June 6 showed only a very mild reddening of the conjunctiva and a trace of exudate along the lid margins. Inclusions were still present.

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CHILDREN'S HOSPITAL

ERYTHEMA EXUDATIVUM MULTIFORME WITH OPHTHALMIA AND STOMATITIS

Report of Two Cases in Children With Certain Observations on Histopathology and Animal Inoculation

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ERYTHEMA exudativum multiforme, as first described by von Hebra,[1] is characterized by an eruption (macules, papules, or vesicles) of the face, neck, and extensor surfaces of the hands, forearms and legs. Von Hebra emphasized the absence of constitutional symptoms. More recently, dermatologists[2-8] have recognized a rare form of the disease which involves, in addition, lesions of the mucous membranes (which may precede those of the skin) and manifestations of intoxication. The disease often recurs. Ormsby[8] states that "in some cases the symptoms are limited to the mucous membranes only, in certain recurrences." The etiology is still obscure. Stevens and Johnson,[9] in 1922, reported two cases of this rare condition, which stimulated others to report similar cases.[10-12]

It is the purpose of the present paper to present two cases of the rare form[9] of erythema exudativum multiforme in children, one of which was recurrent, together with certain observations on the histopathology and the effects following animal inoculation of vesicular fluid and of blood derived from an active case.

Case 1.*—A. L., No. 84231, a Jewish boy, aged twelve years, was admitted to the hospital Dec. 30, 1933, with an exanthem, stomatitis, ophthalmia, fever, and generalized malaise that had developed during the preceding twenty-four hours.

Family History.—The parents and two siblings were well.

Past History.—The general health of the patient had been good except for recurring attacks of rhinitis each winter. His development during infancy was normal; later he acquired the Fröhlich type of adiposity. He had measles at two years, pertussis and chickenpox at four years, and was vaccinated against smallpox at five years.

Present History.—The patient was in good health until nine days before admission to the hospital. At that time a localized swelling confined to the left side of his face appeared; it was diagnosed as parotitis. During the next three days this had largely regressed. The second day before admission marked the onset of a sore throat which rapidly became acute, with malaise and fever. He refused all nourishment the day before admission. On the development of ophthalmia, he was brought to the hospital.

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*We acknowledge the assistance of Dr. A. R. McFarland, who diagnosed this case.

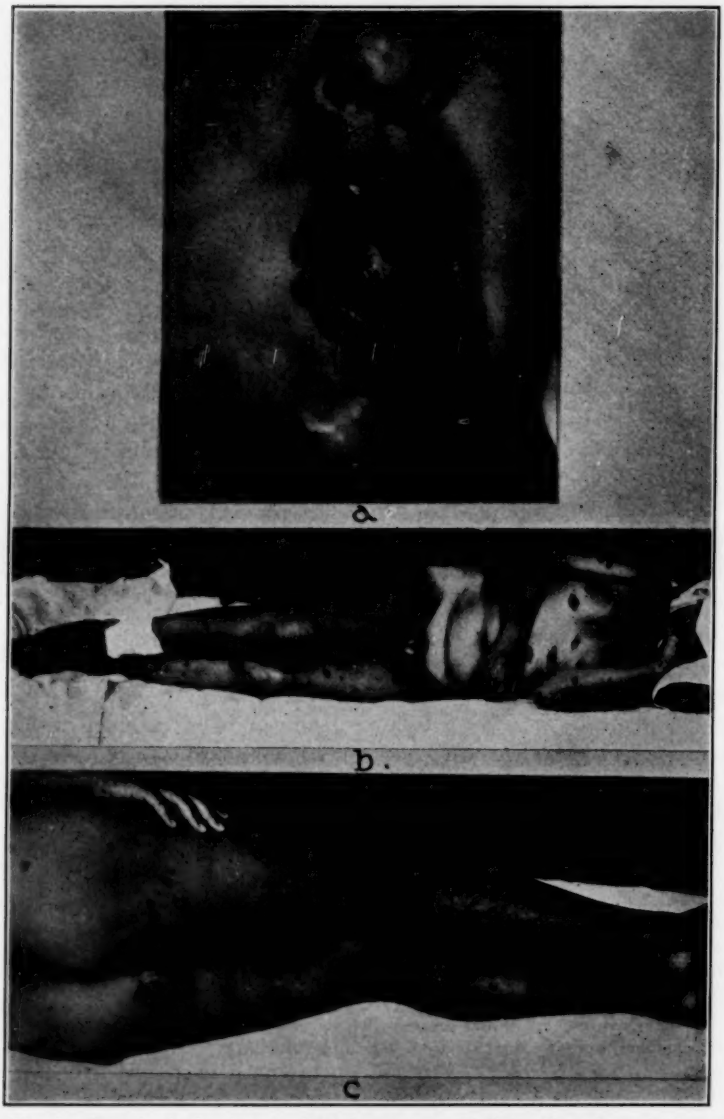

Fig. 1.—Case 1. A. L., boy aged twelve years. Photographs taken at time of second admission: *a*, showing involvement of mucous membranes; *b*, and *c*, showing multiform unilocular umbilicated vesicular lesions some of which have a hemorrhagic periphery.

Fig. 2.—Case 1. A. L., boy aged twelve years. Photomicrographs of lesions removed for biopsy: *a*, showing general gross configuration of typical skin lesion (×6.5); *b*, section through edge of lesion showing indistinct line of demarcation and accumulation of vesicular fluid (×60); *c*, higher power (×220) showing separation of overlying layers from the stratum germinativum.

Physical Examination on Admission.—Temperature 39.7° C., pulse rate, 144; respiration, 32. The patient was an acutely ill Jewish boy with the Fröhlich type of obesity. The skin was warm; no eruption was evident. Marked infection of the conjunctivae was accompanied by a moderate amount of purulent discharge. The nose and eardrums were normal. The lips were swollen, crusted, and cracked. Of the numerous bullous lesions on the soft palate and buccal mucosa, many were unbroken, whereas several had ulcerated. The tongue was coated. Both tonsils were of moderate size and red, and on the uvular surface of the left tonsil a white patch was seen. The left parotid gland was slightly swollen. There was also moderate swelling and tenderness at each angle of the jaw and in the submental region. The heart and lungs were normal. The abdomen was obese; no organs were palpable. The genitals were infantile. No abnormal reflexes were elicited.

Laboratory Findings.—Blood studies on admission revealed red blood cells, 6,600,000; hemoglobin, 15.5 gm.; white blood cells, 17,800—polymorphonuclears, 74 per cent, basophiles, 1 per cent, lymphocytes, 22 per cent; monocytes, 3 per cent. Five days after admission white blood cells numbered 6,200; polymorphonuclears, 47 per cent; basophiles, 1 per cent; eosinophiles, 6 per cent; lymphocytes, 39 per cent; and monocytes, 7 per cent.

The blood Wassermann test was negative.

Blood cultures on the first and fifth days following admission were negative.

Urine on admission showed 1+ albumin. Other analyses were negative.

Nose and throat cultures were negative for *Corynebacterium diphtheriae.* Thirty per cent of the colonies in the throat culture were *Streptococcus hemolyticus.*

A smear from mouth lesions showed no fusiform bacilli or spirochetes, and cultures from purulent conjunctival discharge showed that the predominating organism was *Staphylococcus aureus.*

Schick, Dick, and Mantoux (0.1 mg.) tests were negative.

Course.—On the sixth day after the onset of the illness, several small, round, vesicular lesions were noted on the chest and extremities. These enlarged and, together with the new ones which appeared during the next few days, became bluish in color with a surrounding area of erythema (1 to 4 cm. in diameter). A profuse purulent exudate drained from both eyes. Blanching with adrenaline demonstrated that the infection was limited to the conjunctivae; the corneae remained clear. Treatment of the eyes consisted in the conjunctival instillation of a solution of metaphen (1:2,500) every three hours, preceded and followed by boric acid irrigations. Definite improvement was noted six days after treatment was started. Over a period of nine days the temperature gradually subsided from 40.5° C. to normal. The skin lesions faded with slight pustulation and no scarring.

The patient was entirely well for six months (until June 27, 1934) when, following an afternoon of swimming, he again complained of sore throat. This continued to be slight for several days. On July 3 he complained of malaise. A "small lesion" was seen by a local physician on one tonsil that day. Others appeared in the mouth during the night and his temperature rose. He was admitted to the hospital on July 4.

Physical Examination on Admission.—Temperature was 39.4° C.; pulse rate, 144; respiration, 35; blood pressure, 124/90. The patient again appeared acutely ill and uncomfortable. The conjunctivae were moderately injected, and a small amount of purulent exudate was present. Both palpebral and bulbar conjunctivae were involved, especially at the periphery. The lips were moderately swollen, and there was a large bleb at the left corner of the mouth. The entire buccal mucosa, tongue, palate, and pharynx were covered by a thick, white coat through which no vesicles or ulcers could be seen. Swallowing was painful. The anterior and posterior cervical lymph nodes were tender and moderately swollen, with some swelling of the surrounding soft tissues. The skin was clear.

Laboratory Findings.—Blood studies on admission showed red blood cells, 4,870,000; hemoglobin, 15 gm.; white blood cells, 12,450—polymorphonuclears, 85 per cent; lymphocytes, 11 per cent; and monocytes, 4 per cent. Seven days after admission a count showed red blood cells, 4,800,000; hemoglobin, 12.5 gm.; white blood cells, 10,800; polymorphonuclears, 64 per cent, eosinophiles, 1 per cent, lymphocytes, 28 per cent; and monocytes, 7 per cent.

The blood Wassermann test was negative.

Aerobic blood culture on the fourth day following admission showed no growth, and an anaerobic culture on the seventh day showed no growth.

The urine, on admission, contained albumin. Other analyses were negative.

Nose and throat cultures were negative for *Corynebacterium diphtheriae* and hemolytic streptococci.

Smear from mouth lesions was negative for Vincent's organisms.

Vesicle cultures on third day showed no growth. On fourth day they showed a few colonies of *Staphylococcus aureus.*

Schick, Dick (also with heat-stabile or endogenous streptococcic toxin), and Mantoux skin tests were negative.

Other laboratory work, bearing on adiposity, is omitted.

Biopsy Examination.—A recently formed vesicular lesion was removed, placed in Zenker's acetic 5 per cent fixative for twenty-four hours, and then stained with hematoxylin eosin and Giemsa stains.

Histologic examination showed pigmented skin which was hyperplastic around the periphery of the lesion. The overlying layers of the epidermis were compressed and elevated from the underlying stratum germinativum by an accumulation of coagulated fluid in which strands of fibrin and an occasional polymorphonuclear cell and lymphocytes were present. The entire epithelium was intact with no evidence of necrosis and ulceration. The blood vessels of the corium showed evidence of dilatation with perivascular cellular infiltration and proliferation. Scattered throughout the corium were occasional mononuclear and plasma cells. No multinucleated cells were seen. No inclusion bodies suggestive of virus action were present.

Course.—On the day of admission (July 4) or the second day of fever, the patient began to complain of difficulty in urination, and at that time several blebs were noted on his penis. Later that day vesicular lesions appeared on the chest. Within twenty-four hours, the whole body was covered by unilocular, vesicular lesions 0.5 cm. to 1 cm. in diameter. Some were surrounded by small areas of erythema. Two days later they were hemorrhagic, and the zones of hemorrhage enlarged. Cultures from the vesicles at this stage showed no growth. One lesion removed for biopsy at this time is described above. Meanwhile, the purulent discharge from the eyes had become very profuse and necessitated hourly irrigations. The corneae did not become involved. Atropine ointment was used. On July 9 the temperature was normal (six days after the onset of fever). The lesions dried and desquamated without scarring.

After the patient had recovered, a search was made for foci of infection. X-ray films of the sinuses, teeth, and chest were negative. The tonsils were small, but since these episodes were preceded by sore throats, tonsillectomy and adenoidectomy were done two weeks after recovery. No histopathologic examination was made of the tonsils.

The patient had an acute attack of appendicitis with appendectomy and uneventful recovery during October, 1935. Histopathologic examination of the appendix revealed an acute inflammatory process as evidenced by closure of the lumen and infiltration of all layers with polymorphonuclear cells. A fibrinous exudate was present on the serosa.

He was well until June 3, 1936. On that day rhinitis and slight cough began (the first since July, 1934). On June 10 his throat became sore and lesions began to appear in his mouth similar to those he had had before. He was brought to the out-patient department for examination and treatment. His mouth and throat showed many vesicular lesions of varying size, some already broken. He had no fever, malaise, skin lesions, or conjunctivitis. He was given directions for sodium perborate mouth washes, nonirritating foods and aspirin, 0.65 gm. t.i.d. The mouth lesions persisted for five days, then cleared rapidly without the appearance of other signs or symptoms. No laboratory work was done.

CASE 2.*—V. R., No. 114042, an Italian girl, aged fifteen years, was admitted to the hospital April 9, 1936, with an exanthem, stomatitis, ophthalmia, fever, and malaise of eight days' duration.

Family History.—The parents and siblings were well.

Past History.—Her health had always been good. She had had only the usual childhood infections. Until tonsillectomy at ten years, she had numerous sore throats, but none since. There was no history of allergy or of rheumatic fever in the patient or her family.

Present History.—The patient was in good health until eight days before admission to the hospital (April 1), when she developed blisters on her lips. The blisters later appeared in her mouth and throat. Fever and a moderate diarrhea began at this time. On April 6 she developed red, flat lesions on her hands, forearms, and legs. These increased in number during three days and developed vesicles. They itched slightly. She had no chills, nor vomiting. No medication was given at home.

Physical Examination.—On admission the temperature was 38.6° C.; pulse rate, 88; respiration, 20; and blood pressure, 110/60. The patient was a well-developed girl of fifteen years, acutely ill and drowsy. Large, rosy eruptions were present over the forearms and hands. Smaller ones were present on both legs and ankles, topped with vesicles. The larger lesions were umbilicated, the vesicles forming an irregular circinated border, the fluid clear and amber. There was no hemorrhage, and the erythema blanched on pressure. The ears and nose were normal. The conjunctivae were injected. A small amount of purulent exudate was present. There was slight photophobia. The corneae were clear, and the pupils reacted well. The lips were swollen; bleeding, shallow, necrotic irregular ulcers covered the entire buccal mucous membrane. The hard palate was covered with small vesicles, and the tongue showed eroded ulcers on the margins. The uvula was edematous. The tonsils were out. The thyroid was not enlarged. Small, firm, nontender submaxillary and posterior cervical nodes were palpable. No pathologic changes were found in the chest. The pulse was from 90 to 110 per minute. The abdomen was normal Pelvic and rectal examinations were negative. The extremities which showed sluggish reflexes were otherwise normal.

Laboratory Findings.—Blood studies on admission showed red blood cells, 4,990,000; hemoglobin, 14 gm.; white blood cells, 9,800—polymorphonuclears, 70 per cent, eosinophiles, 1 per cent, basophiles, 1 per cent, lymphocytes, 23 per cent, and monocytes, 3 per cent.

Five days after admission the results of a study were white blood cells 10,350—polymorphonuclears, 80 per cent, lymphocytes, 20 per cent.

The blood Wassermann was negative.

Sheep cell agglutination test (April 10) resulted in no agglutination.

The urine was entirely normal on two examinations.

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*We are indebted to Dr. W. S. McCann, Professor of Medicine, for his permission to include Case 2, and to Dr. H. C. Shaw, who established the diagnosis and outlined the treatment of this case.

The electrocardiographic findings were as follows: Rate, 80; P-R interval, 0.29 sec.; QRS interval, 0.07 sec.; QRS slurred in Leads I and III; S-T elevated in Leads I and II; T_3, low. Ventricular extrasystoles were noted.

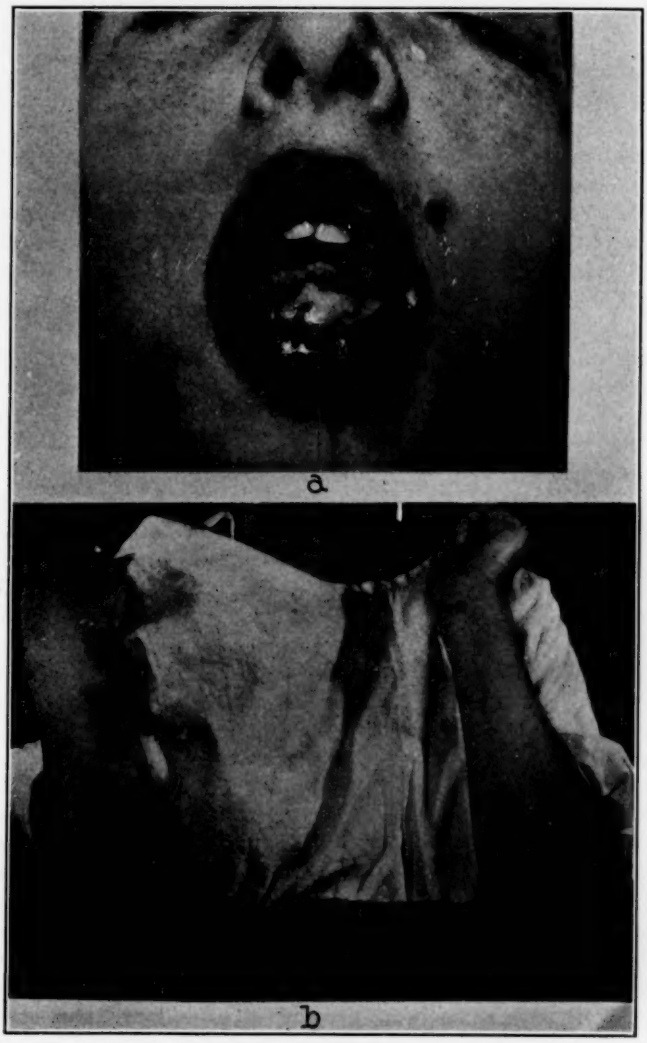

Fig. 3.—Case 2. V. R., girl aged fifteen years: *a*, showing involvement of mucous membranes; *b*, showing irregular vesicular lesions.

Course.—The patient's temperature ranged from 39 to 38° C. during the first four days after admission (ninth to thirteenth days of illness) and was then normal. Sodium perborate mouth washes were given every three hours, and boric acid eye irrigations were given every two hours during the day. Sodium salicylate, 4 gm., and

sodium bicarbonate, 2 gm., were given every two hours during the day. The marked improvement following the administration of salicylates is noteworthy. By April 15 all of the lesions were beginning to fade, and the patient was able to eat solid food. The patient was discharged with all lesions practically healed on April 19.

EXPERIMENTAL

(Material taken from lesions of second admission in Case 1.)

The unknown etiology of this disease makes any observations based on animal experimentation worthy of mention.

In an attempt to determine if the vesicular fluid contained any transmissible agent, one rabbit, one guinea pig, and six Swiss mice were inoculated by the intracerebral route. The rabbit had a temperature of 40.3° C. on the seventh day only. No untoward signs were noted in the guinea pig or mice.

Four mice were given the fluid by both intracerebral and intraperitoneal routes without visible effect.

Two guinea pigs were injected intradermally and into the pads without detectable effects.

Sutton and Sutton[6] believe that, with the evidence now at our disposal, an explanation based on analogies with the anaphylactic phenomenon is the most plausible one that has yet been advanced. That the observed clinical manifestations were of an allergic, or possibly toxic nature, possibly found some support in the following observations.

Three days following the initial inoculations, a small amount of fluid was obtained from the few vesicular lesions that remained. By this time the majority of the lesions had become papulopustular with an irregular circumferential hemorrhagic periphery.

Two rabbits were each inoculated intravenously with 4 c.c. of the patient's serum. Twenty-four hours later 0.15 c.c. of the vesicular fluid was similarly injected. No untoward effects were observed.

Two other rabbits were each inoculated intravenously with 0.15 c.c. of vesicular fluid. This was to be followed in twenty-four hours by 4 c.c. of the patient's serum by the same route. Within an hour following the first injection, both rabbits were in acute distress as evidenced by their humped-up appearance, difficulty in respiration, and cyanosis. One of them died within four hours. An autopsy revealed no abnormalities other than marked bilateral pulmonary edema with the heart in diastole. The second rabbit died two days later. Autopsy at that time revealed a bilateral hemorrhagic bronchopneumonia. Attempted transfer passage using liver, spleen, kidney, lung, and brain suspensions resulted in no demonstrable effect in three of four rabbits. The fourth had a febrile reaction of 41° C. with death in twenty-four hours. Using similarly prepared suspensions, further transfer to six additional rabbits was entirely without effect.

The postmortem findings described are similar to those of rabbits dying from anaphylactic shock.

Unfortunately, source material from a patient for further study was not available. Naturally, on the basis of such limited findings, we do not feel that we can form any opinion as to the mechanism involved. These limited findings are reported herewith so that when a similar case presents itself elsewhere, further investigation along these lines may be instigated.

SUMMARY

The clinical features of two cases of erythema exudativum multiforme in children are described. In both instances, the skin and mucous membranes were involved. There was multiform exanthem, stomatitis, ophthalmia, and constitutional reaction. One case was recurrent. Observations are recorded on the histopathology of biopsy material and on certain findings based on animal inoculation.

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A STUDY OF THE PROPHYLACTIC EFFECTS OF PERTUSSIS VACCINE

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IN APRIL, 1934, fifty children at the Summit County Children's Home, who had never had pertussis, were given pertussis vaccine (Sauer). Fifty other children of comparative age in the same institution, who also had never had pertussis, were used as controls. Each child vaccinated received the complete immunization as recommended by Dr. L. Sauer. The initial dose consisted of 1 c.c. of the vaccine injected hypodermically in each arm; seven days later, 1½ c.c. were injected in each arm; seven days after the second dose, 1½ c.c. were injected in each arm, making a total dosage given of 8 c.c. within a period of two weeks. No unusual local or systemic reactions followed the injections.

The Summit County Children's Home receives the orphans and wards from the Courts of Summit County. The children are usually kept over a long period of time which gives the opportunity to follow and study them. They attend the public schools of the city and thus are exposed to all of the contagious diseases prevalent in the community.

In April, 1936, two years after the pertussis vaccine had been given an epidemic of pertussis broke out in one of the departments in which 29 children between the ages of three and seven years were living. This department was immediately isolated and no child was permitted to leave except to exercise on the playground when the other children of the Home were in school or at their meals.

The 29 children in the department under observation were classified into three groups. The first was made up of 12 children who had never had pertussis, and had not received pertussis vaccine; the second group consisted of 9 children who had received complete pertussis immunization two years previously; the third comprised 8 children in the department who had had pertussis. Five of the 8 cases (Nos. 22-25 and 29) had pertussis at some previous date in the Children's Home. Cases 26, 27, and 28 had definite attacks of pertussis before entering the institution.

It is of interest to note that the disease remained limited to this department and no other case developed in the institution. During the entire period of observation, which lasted over seven weeks, all the children in the quarantined department played together; had their meals in the same refectory and slept in the same dormitory. This provided repeated, severe multiple daily exposures for all of the children and should be a

far greater test of the efficacy of the vaccine than could be obtained from a series of cases observed in individual families where mild, infrequent exposures normally would be the rule.

The children under observation were supervised by nurses; two being on duty during the day and one at night. The nurses neither knew who had been given pertussis vaccine nor why the experiment was being conducted, thus eliminating all personal bias from the study.

During the first week of the observation the nurses, at the end of the day, gave their impression of each individual's coughing. If coughing had occurred they recorded it as hard or light. After one week it was realized that no definite information could be obtained with this method of evaluation. The nurses were then requested to chart with a vertical line each paroxysm. The length of the line denoted the severity of the paroxysm and we recognized four gradations from mild to severe as can be seen on the accompanying charts. The letter *W* was used when a definite inspiratory whoop occurred. The nurses carried the chart with them wherever the children went, out on the playground, in the refectory and into the dormitory for naps or for the night's rest. No medication was administered to the children during the entire course of the disease except codeine, which was given very sparingly and only to the more severe cases, especially at night.

A glance at the accompanying chart shows better than anyone can narrate the course and severity of the various groups to the common infection, pertussis. No detailed study seems necessary and will not be attempted in reviewing the results, for the answer is so obvious.

Group 1, those cases who never had pertussis nor received the prophylactic vaccine, all ran a typical course. Ten of the 12 cases had a paroxysmal cough throughout the entire seven weeks of the observation, while two of the cases (Nos. 6 and 8) were content with but five weeks' coughing. On the whole the cases were but moderately severe.

Group 2, those children who had the pertussis vaccine two years previously, had a comparatively easy time. Three weeks was the average length of the attack for 6 of the 9 cases. One (No. 19), coughed but one week; No. 20 coughed but one day and No. 21 was without a coughing paroxysm during the entire period of observation. On the whole as can be seen from the chart, the paroxysms were notably less in number and severity as compared with Group 1.

All of Group 3, those children who had a positive history of pertussis previous to the study, had coughing paroxysms. Six coughed for periods averaging about three weeks, while cases Nos. 24 and 28 coughed but one week. The paroxysms were neither so frequent nor severe as Group 1, but it is extremely interesting to note that of this group not one case escaped having a mild form of the disease, and certainly as a group, coughed as much as the children protected by the vaccine.

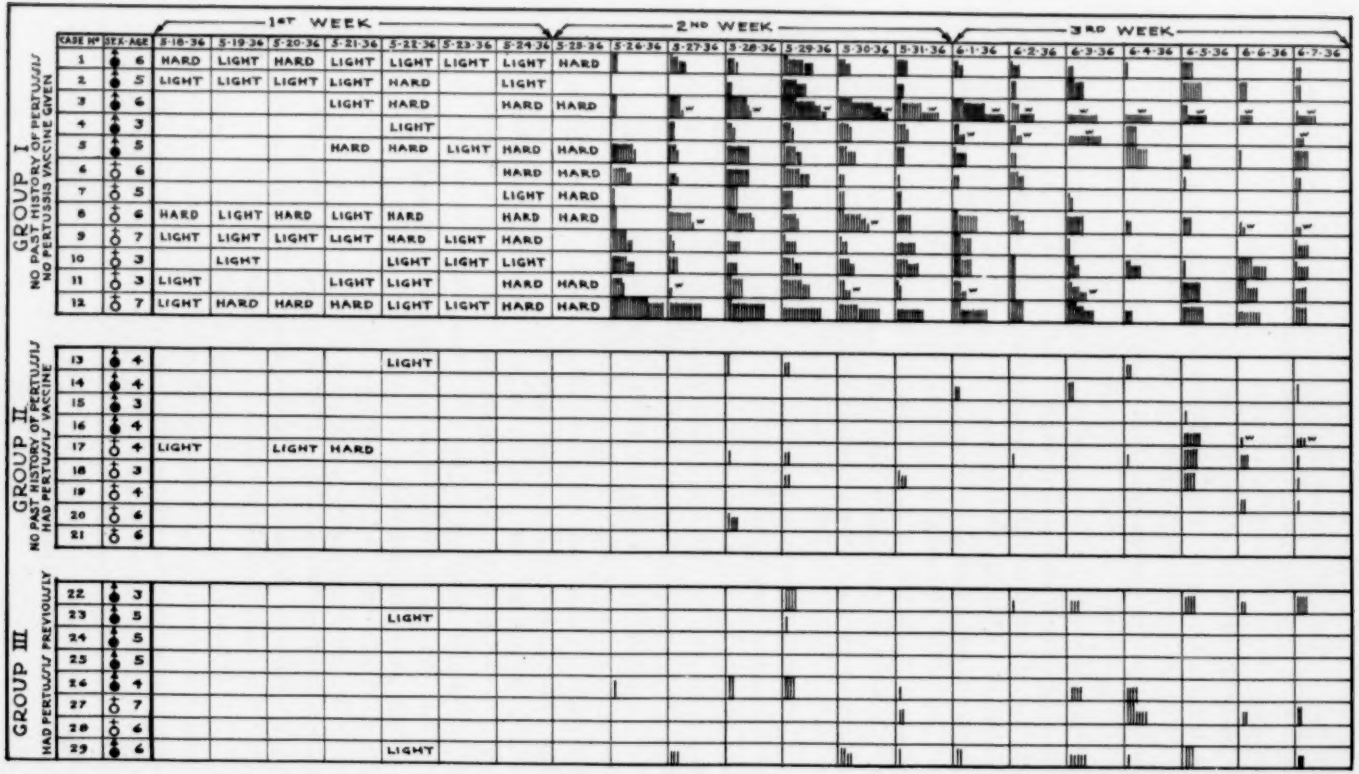
1ST WEEK
2ND WEEK
3RD WEEK
CASE Nº
SEX-AGE
5-18-36
5-19-36
5-20-36
5-21-36
5-22-36
5-23-36
5-24-36
5-25-36
5-26-36
5-27-36
5-28-36
5-29-36
5-30-36
5-31-36
6-1-36
6-2-36
6-3-36
6-4-36
6-5-36
6-6-36
6-7-36
GROUP I
NO PAST HISTORY OF PERTUSSIS
NO PERTUSSIS VACCINE GIVEN
GROUP II
NO PAST HISTORY OF PERTUSSIS
HAD PERTUSSIS VACCINE
GROUP III
HAD PERTUSSIS PREVIOUSLY

Chart 1.

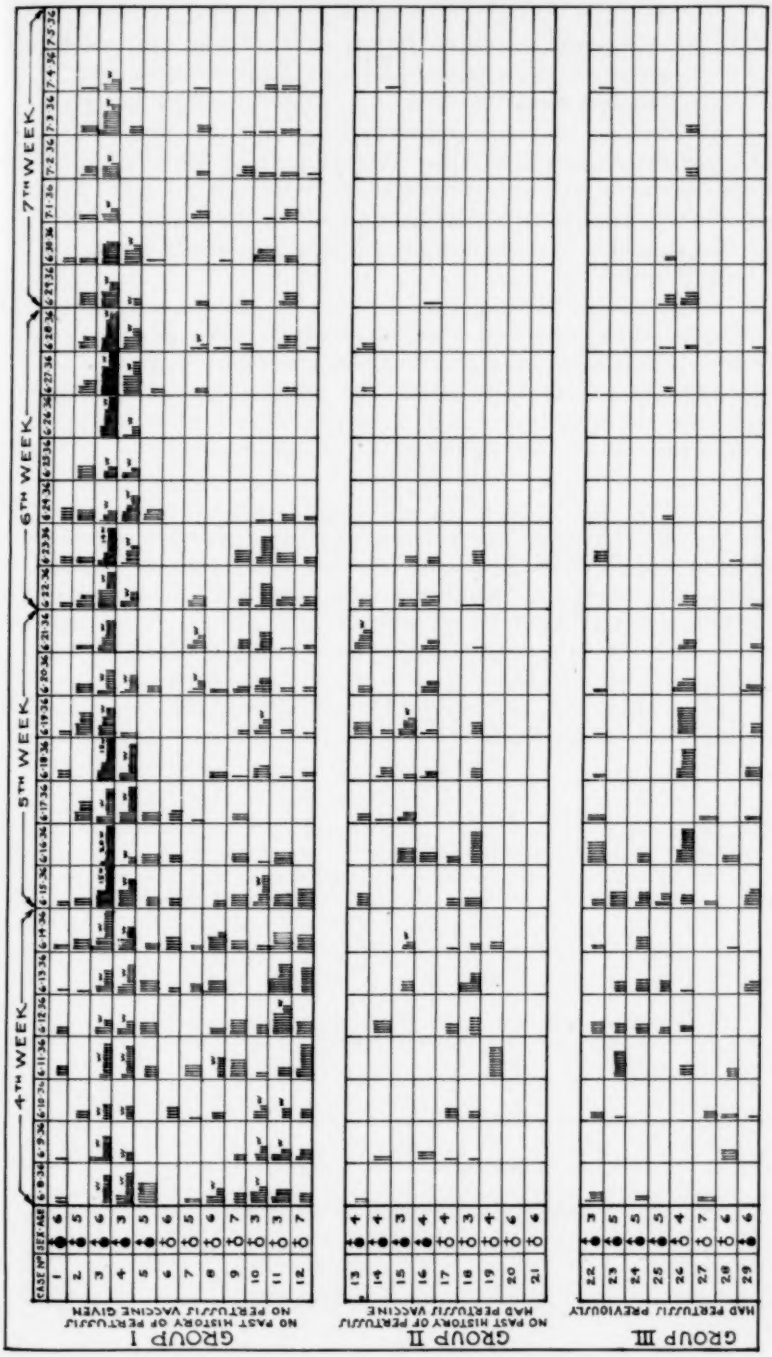

Chart 1.—Cont'd.

A study of the chart reveals the fact that the children not protected by the vaccine or a former attack of pertussis, had what we recognize as a typical attack and course of pertussis. The group immunized by the vaccine, had an extremely mild form of the disease and in one instance, was seemingly completely protected from the disease. The third group who had pertussis previously, developed a mild secondary attack of the disease in all instances. This is in direct variance to the usually accepted idea that an attack of pertussis confers a lasting immunity in the vast majority of cases.

No complications were encountered in any of the cases during the seven weeks of the study. Unfortunately, no laboratory work such as cough plate cultures or blood counts, could be attempted because of the lack of facilities, time, and finances. This would have confirmed some points that may be in doubt. It is hoped that this will be attempted in the future, should the occasion arise for a similar study.

CONCLUSIONS

1. Pertussis vaccine (Sauer) confers a relative immunity within a period of two years from the time of administration and the results would seem to justify the continuance of its use.

2. Immunity resulting from the use of pertussis vaccine (Sauer) is as effective as a previous attack of the disease in conferring immunity upon children.

3. An attack of pertussis does not confer complete immunity from a mild recurrence of the disease.

HODGKIN'S DISEASE WITH TERMINAL EOSINOPHILIA OCCURRING IN A NEGRO CHILD WITH SICKLEMIA

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THE occurrence of Hodgkin's disease in a colored patient belonging to a family displaying the sickling tendency may be but a simple coincidence. Nevertheless, such a combination is so unusual that it warrants the following case report. In the comprehensive reviews of Hodgkin's disease by Symmers (1924), Simonds (1926), and Wallhauser (1933), no mention is made of any instance in which this particular combination occurred. Furthermore, the presence of true blood eosinophilia in Hodgkin's disease is now regarded as a rarity, even though tissue eosinophilia is very frequently encountered. Sears, in 1932, was able to collect from the literature only thirteen cases of Hodgkin's disease with peripheral eosinophilia, the only cases not included in his tabulation being the earlier reports by Glanzmann (1915) and by Steiger (1915), and those recently presented by Holzknecht (1932) and by Coburn and Pritchard (1934). Moreover, the present case embodies certain histologic features which require a new interpretation, particularly with reference to the histogenesis of the mononuclear and multinuclear giant cells regarded as pathognomonic of the disease. The interpretation herein offered is suggested as a possible basis for reconsideration of Hodgkin's disease as to its proper nosologic position.

REPORT OF CASE

T. P., a fourteen-year-old negro male, was admitted to Provident Hospital, Chicago, July 13, 1935, with complaints of (1) shortness of breath, (2) cough, and (3) swelling in left side of the neck. The onset of the present illness was thought to have begun when the child fell about 10 or 15 feet from an iron pole he was attempting to climb some two months previous to his hospital admission. The patient landed face downward but did not become unconscious. However, he did vomit fresh blood shortly afterward. A "lump" was present in the right chest wall for about one week following the accident following which it disappeared spontaneously. Three weeks later, however, a large swelling making its appearance at the base of the left side of the neck brought the patient to the out-patient clinic of the hospital.

Past History.—The child's birth, in Provident Hospital, April 24, 1921, was normal; he was breast fed for nine months, sat up at six months, walked at ten months, and talked at eighteen months, though never plainly. Previous illnesses were an attack of pneumonia at ten months, and measles followed by chickenpox at four years. The interim history was irrelevant, the several clinic visits up to the age of thirteen being chiefly for dental caries and behavior problems.

Out-patient examination (Chest Clinic) revealed "dullness in the midline from the clavicle to the diaphragm, extending laterally in both directions well into the

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lung fields; the breath sounds were very distant.'' Fluoroscopic examination at the time confirmed these findings and a clinical diagnosis of ''mediastinal tumor, probably lymphosarcoma'' was made. Three days later a roentgenogram (Fig. 1) enabled the roentgenologist (Dr. B. W. Anthony) to make the following report: (1) Massive mediastinal tumor, in all probability a malignant lymphoma; (2) aorta not visualized, likewise the heart not outlined; (3) low grade but frank left hydrothorax and thickening of the left pleura.

Family History.—Father died of epidemic meningitis; mother ''thinks she has a tumor of the uterus.'' Four siblings were born at full term; there were no miscarriages. Patient's maternal aunt and great-grandfather died of tuberculosis.

Physical Examination.—The following positive findings were obtained upon admission: (1) Dyspnea and marked orthopnea; (2) dry brassy cough; (3) occasional choking sensation and difficulty in swallowing; (4) soft bilateral swelling of the neck anteriorly; (5) dullness over the entire thorax bounded by the clavicle above, the diaphragm below, and the midclavicular lines on both sides; (6) markedly

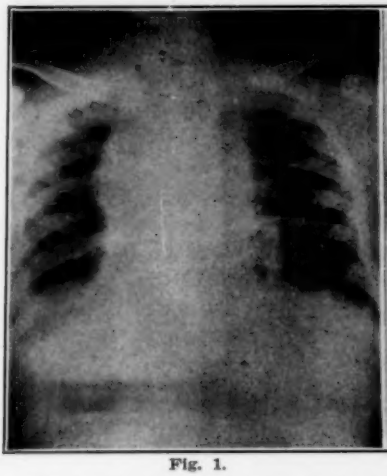

Fig. 1.

Fig. 2.

Fig. 1.—Roentgenogram of the chest (July 16, 1935).

Fig. 2.—Photograph of the mediastinal mass removed at autopsy, showing its relation to the heart and the lungs (Aug. 13, 1935).

diminished breath sounds over the area of dullness; (7) indistinct apical heart beat; and (8) increased anteroposterior diameter of the chest. Temperature was 100.2° F., pulse rate, 65; and respiration, 35 per minute; blood pressure registered 140/78.

Laboratory studies showed the urine to be negative and the sputum negative for tubercle bacilli. Routine blood counts are tabulated in Table I. Coagulation time

TABLE I

SUMMARY OF BLOOD COUNTS

DATE	R.B.C.	HB % (SAHLI)	W.B.C.	P	L	M	E	B
7/23/35	4.05	80	7,800	68	28	2	2	0
7/28/35	4.50	75	14,300	–	–	–	–	–
8/ 6/35	5.10	55	25,600	–	–	–	40	–
8/ 9/35	4.80	60	26,000	43	3	5	47	2

was 3.5 minutes; bleeding time, 4 minutes. Blood Wassermann and Kahn tests were negative. The Beck and Hertz method (1935), as well as the standard cover-slip method, for testing of the sickling tendency of the red blood corpuscles was applied to this patient's erythrocytes, and both were markedly positive in twelve hours (Fig. 3). The same methods of study were then applied to the red blood cells of the mother, which were found also to be 50 per cent positive in twenty-four hours. Other members of the family were not tested.

Biopsy of a lymph gland from the right axilla was made on July 27, 1935, with the following report: "The microscopic study reveals no characteristic pathologic picture. There is a marked increase of eosinophiles scattered throughout the gland. There is also an increase of polymorphonuclear leucocytes above the normal. The red blood corpuscles show sickling in the blood vessels." (Fig. 4.)

Because of increasing dyspnea and edema of both legs, a second roentgenographic examination was made (Aug. 6, 1935) and revealed "moderate increase in size of

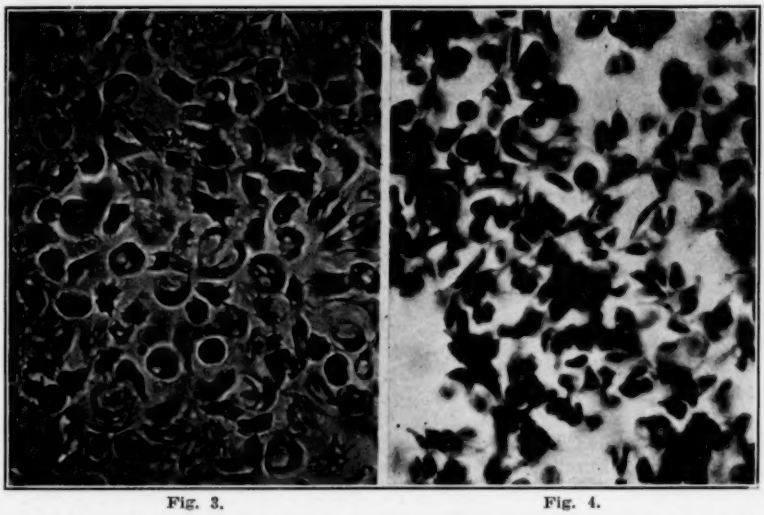

Fig. 3. Fig. 4.

Fig. 3.—Photomicrograph of the patient's erythrocytes at twelve hours (standard cover-slip method) (×1500).

Fig. 4.—Photomicrograph of blood clot within a capillary of the lymph node removed by biopsy, showing the presence of numerous sickle cells (×1500).

the mediastinal tumor mass; increase in the pleural effusion in the right chest cavity." The day following this report a thoracentesis of the left pleural cavity was done and 450 c.c. of dark straw-colored thick fluid removed. The fluid clotted so very quickly after removal that the specific gravity could not be determined. Microscopic examination revealed (1) many erythrocytes showing macrocytosis and polychromatophilia, nucleated red cells, and cells incompletely sickled; (2) the leucocytes consisting of many large cells with a single large round nucleus and a pale agranular cytoplasm, and many granular forms with bilobed nuclei resembling eosinophiles. The cholesterol content of this fluid was reported to be 615 mg. per cent, and the culture negative. Another roentgenogram made immediately after thoracentesis disclosed no additional pathology except for a diminished amount of fluid in the left pleural cavity. Because of the rapidly progressing weakness of the patient, no further investigations were attempted. Death ensued on Aug. 12, 1935.

Clinical Course.—On admission, the patient was found to be well nourished, very alert, little disturbed by his dyspnea, orthopnea, or brassy cough. The usual cachexia and anemia commonly reported in cases of this type were at no time seen in this patient. Except for a slight epistaxis and a somewhat increasing orthopnea, the patient's condition was unchanged until the twelfth day after admission, at which time he first complained of pain in the ankles, and examination of the latter revealed a pitting edema not previously noted. The dyspnea and orthopnea increased to the extent that the patient was unable to obtain any relief except by sitting in a wheel chair and bending well forward. He could not be induced to leave the chair for the bed. The swelling of the ankles spread so rapidly upward involving the legs and abdomen that within three days he was unable to move his lower extremities, and all sensation was abolished below the level of the hip. The thoracentesis above referred to was done four days before the patient died, at which time such alarming symptoms as incontinence, cyanosis, and anasarca were already present. Removal of the fluid from his left pleural cavity caused a temporary relief of symptoms for about twenty-four hours, following which cyanosis and dyspnea reappeared even more markedly than before. Until the seventh day before his death, when it fell to 98° F., where it remained until the end, his temperature during the entire stay in the hospital ranged between 99° and 100° F., except for a rise on two occasions to 101° F. The pulse rate was from 60 to 65 per minute on admission, but increased soon afterward to 120 to 140 per minute. Before death it fluctuated between 80 and 180 per minute. One deep x-ray therapy (300 r.) over the upper mediastinum through the back was given on the day before his death.

Autopsy Protocol.—The postmortem examination, made by Dr. M. M. Shaw thirty hours after death, resulted in the following anatomic diagnoses: (1) Mediastinal lymphogranulomatosis Hodgkini with spread to the lungs and the pericardium; (2) bilateral hydrothorax; (3) parenchymatous degeneration of the myocardium; (4) parenchymatous degeneration of the kidneys; (5) induration of the spleen; (6) marked anasarca, especially of the upper extremities, the face and the neck; (7) sickle-cell anemia.

The more important gross and microscopic findings are summarized as follows:

Pleural Cavities.—The removal of the sternum was difficult because of its adherence to the underlying mediastinal mass. Both pleural surfaces were smooth and the cavities contained about 300 to 350 c.c. of a clear, straw-colored fluid. A large mediastinal mass extended laterally into both pleural cavities. The lungs were collapsed.

Pericardial Cavity.—Though compressed, the pericardial cavity contained a straw-colored fluid somewhat in excess of the normal. The inner surface of the sac was smooth and glistening, but the external surface was studded with numerous nodules varying in size from 0.8 to 3.0 cm. in diameter. The masses, gray white in color, cut with some increase in resistance, revealing a white firm surface with white fibrous bands crossing the substance.

Trachea, Bronchi, and Esophagus.—These structures were surrounded and partially compressed by the mediastinal mass together with the adjacent enlarged lymph nodes. The compression did not cause obstruction. The mucosa of the trachea and bronchi was pale and covered with an increased amount of white mucoid material. The esophagus was compressed and pushed to the right of the midline.

Thyroid and Thymus.—The thyroid, weighing 25 gm., was smooth, lobulated, pale tan in color, and the surface, upon cutting, was glistening. The thymus had undergone physiologic atrophy.

The Heart and Vessels.—The base of the heart was compressed by the mediastinal mass. Its transverse diameter was 8.5 and the longitudinal 10.5 cm. The wall of

the left ventricle was 12 mm. in thickness; the right, 3 mm. The myocardium was pale gray brown and of good consistency. The endocardium was smooth, with no significant valvular changes. The ascending portion and the arch, together with the first part of the descending aorta, as well as the pulmonary arteries, were surrounded by the mass and compressed by it. The aorta was thin-walled, the intima smooth, with no evidence of invasion by the mass.

Mediastinal Mass.—The mediastinal mass, measuring 15 by 15 by 9 cm. in its greatest dimensions, pale gray to pinkish gray in color, was irregular in shape, nodular and very firm. The central portion, more dense than the periphery, was composed of a mass of densely adherent glands indistinguishable in the midportion, but revealing individual lymph nodes at the periphery, measuring 1 to 7 cm. in the greatest diameter. No areas of necrosis, even in the interior of the mass, were present (Fig. 2).

Lungs and Tracheobronchial Nodes.—The lungs were compressed by the fluid in the pleural cavities. Because of the deposits of black pigment, the pleura was blackish gray in color, and was studded with firm, whitish masses similar in consistency and structure to the mediastinal mass. The mucosa of the bronchi was pale and was covered by an excessive amount of mucoid material. The tracheobronchial nodes, much enlarged, formed a part of the tumor mass. The normal parenchyma was replaced by the firm, dense, gray tissue.

Liver, Gallbladder, and Spleen.—The liver, weighing 1,400 gm., was increased in consistency. The capsule was smooth and grayish in color, with rounded edges, and its cut surface revealed distinct lobular markings with a yellowish zone about the central veins. The gallbladder was normal. The spleen, weighing 165 gm., was firm with rounded edges. It cut with some resistance, disclosing a dark purple parenchyma in which the trabeculae themselves were distinct but their follicles indistinct.

The organs of the urogenital system, together with the adrenals and the entire gastrointestinal tract were normal.

Lymph Nodes.—The mediastinal, the tracheobronchial, and the cervical nodes were all enlarged and firm, revealing on cutting the replacement of the parenchyma by the dense hyperplastic gray tumor tissue.

Histology.—The histologic sections of the tumor mass at various locations revealed a specific granuloma composed of epithelioid cells and epithelioid giant cells of the Sternberg-Reed type with varying amounts of fibrous tissue reaction. There were many small round cells with a few plasma cells and a tremendous infiltration of eosinophiles. In areas the eosinophiles were so compact as to give a distinct redness to the section even on gross inspection. Some of the sections showed a granular necrosis with obliteration of the cellular structure and details. This portion took an irregular pale stain with eosin. Some of the lymph glands contained small foci of lymphoid tissue near the periphery, but for the most part were replaced by the tumor tissue. The capsule of the gland was greatly thickened.

The sections of the masses in the lung and in the parietal pericardium were similar in structure, with the fibrous tissue, the epithelioid cells, and the Sternberg-Reed giant cells. In all sections of the granuloma eosinophiles were densely collected.

The small blood vessels and capillaries in these sections were filled with elongated, pointed or sickled erythrocytes.

COMMENT

The association of peripheral eosinophilia with Hodgkin's disease, though an old observation, is so unusual that brief comment may not be amiss. From the time Goldmann (1892) first observed, and Kanter

(1894) and Ziegler (1911) emphasized, an eosinophilic infiltration of lymph nodes in Hodgkin's disease, the impression has been widespread that blood eosinophilia is also characteristic of the disease. Fabian (1910) stated that slight eosinophilia (4 to 6 per cent) in the circulating blood occurs in about one-fourth of the cases. More accurate statistical studies, however, fail to substantiate this impression. In analyzing 108 cases of Hodgkin's disease in children Smith (1934) was led to believe that the blood picture is so relatively inconstant as to be of little diagnostic significance, a conclusion also arrived at by Corbeille (1928) after analyzing 33 cases of childhood Hodgkin's disease. Moreover, Roth and Watkins (1936) in their study of the leucocytic picture in 40 cases of Hodgkin's disease made no comment as to eosinophiles, since their cases all showed a normal eosinophilic percentage.

While blood eosinophilia is of rare occurrence in Hodgkin's disease, it is noteworthy that in the presence of progressive lymphadenopathy the increase in circulating eosinophiles is at least suggestive of the disease. The blood picture in Hodgkin's disease, as pointed out by Bunting (1914) and others, appears to depend primarily upon the duration and stage of the disease, and thus there can be no typical or even characteristic findings either in the total leucocyte count or in the relative percentage of any single strain of blood cells. However, Chevallier (1931), Klima (1931) and Goia (1933) noted that eosinophiles usually increase in number only when the total leucocyte count is elevated, the cases with leucopenia ordinarily showing no deviation from a normal percentage of eosinophiles. Among the cases tabulated by Sears (1932) the lowest total leucocyte count (11,000) was that reported by Weber and Bode (1927), with 50 per cent eosinophiles (absolute number, 5,500), while the highest total count (100,000) was recorded by Stewart (1933), with eosinophiles varying from 72 to 90 per cent (absolute number 72,000 to 90,000). In the case here presented, the initial leucocyte picture was normal both in total and absolute counts, but the terminal picture was characterized by a distinct leucocytosis and outstanding eosinophilia. The absolute number of circulating eosinophiles during the last stage of the disease climbed to 12,000, quite in keeping with the cases reported by Bunting (1914) and by Sibley (1915). Such a remarkable blood picture is seldom encountered in any other disease, the closest resemblance being in chronic myelogenous leucemia (Stillman, 1912), in cases of familial or constitutional eosinophilia (Stewart, 1933) and in the so-called eosinophilic leucemia (Shapiro, 1919; Aubertin and Giroux, 1921). In the present case all these conditions must be considered as possibilities, even though lymphogranuloma is the indisputable diagnosis as judged by the underlying pathology which is discussed below.

The histopathologic changes in the lymph node as seen in the sections prepared from biopsy material consisted mainly in the enlargement of the gland with increased reticulum fibers, the meshes of which were densely infiltrated with eosinophilic and neutrophilic granulocytes. No typical reticulum cells of the Sternberg-Reed type were seen although fibrosis was in evidence. From the histologic examination of the tissue alone the diagnosis of lymphogranuloma was, accordingly, but a presumptive one. Practically every tissue studied at autopsy, however, revealed the true Hodgkin's picture. Not only did the macroscopic findings demonstrate the typical manner in which the disease spreads, but the microscopic appearance of the tissues possessed all such classical characteristics as epithelioid cells and epithelioid giant cells of the Sternberg-Reed type, dense eosinophilic infiltration, granular necrosis, and fibrosis (Fig. 5). The terminal eosinophilia with leucocytosis in the present case constitutes a unique feature of the disease. In the absence of an increase in peripheral eosinophiles the lymph node obtained at biopsy revealed a tremendous eosinophilic infiltration of the gland. One may reasonably assume, therefore, that even in the absence of peripheral eosinophilia the presence of large number of eosinophiles in the lymph gland is, in Hodgkin's disease, quite characteristic.

Numerous authors have commented upon the relation of eosinophilic infiltration in lymphogranulomatous tissue to blood eosinophilia. In noting the large numbers of eosinophilic as well as neutrophilic granulocytes in the lymph nodes Goldmann (1892) believed them to have been derived from similar cells circulating in the blood by means of an underlying mechanism assumed to be that of chemotactic stimulus. Many subsequent observers, notably Symmers (1924), have since adopted this so-called colonization theory, but the present case clearly contradicts this view inasmuch as no increase in eosinophiles occurred in the peripheral blood even while the biopsied lymph node was densely infiltrated with these cells. But later, as the disease progressed, eosinophiles did begin to appear in the blood stream in increasing numbers, until the pronounced eosinophilia marked the terminal picture. Again, the view advanced by Barron (1926) to the effect that eosinophilic infiltration of the nodes coincides with blood eosinophilia is not confirmed by the present case.

This leaves us with only one alternative theory, namely, that the involved lymph nodes, being preeminently organs of blood-formation, are endowed normally with primitive mesenchymal cells in the form of undifferentiated reticulum cells which, when acted upon by some pathologic stimulus differentiate not only into lymphocytes as naturally occurring in lymph glands, but also into the myeloid cells normally present in the bone marrow. This possibility of a local origin of granulocytes in Hodgkin's lymph nodes was first suggested by

Kidd and Turnbull (1908), who particularly noted the presence of large numbers of mononuclear eosinophile cells (eosinophilic myelocytes) and eosinophilic micromyelocytes. Similar observations have since been made by others. In the case here presented, the periphery of the lymph nodes still retained some evidence of normal lymphopoiesis, although here also eosinophilic infiltration was so great that the entire tissue in these areas had a reddish appearance on gross inspection. The microscopic picture of the lymph node in these areas was that of a veritable myeloid metaplasia. In other words, the pathologic stimulation of the lymph nodes in Hodgkin's disease results in the extramedullary myelopoiesis of the affected tissue. We may

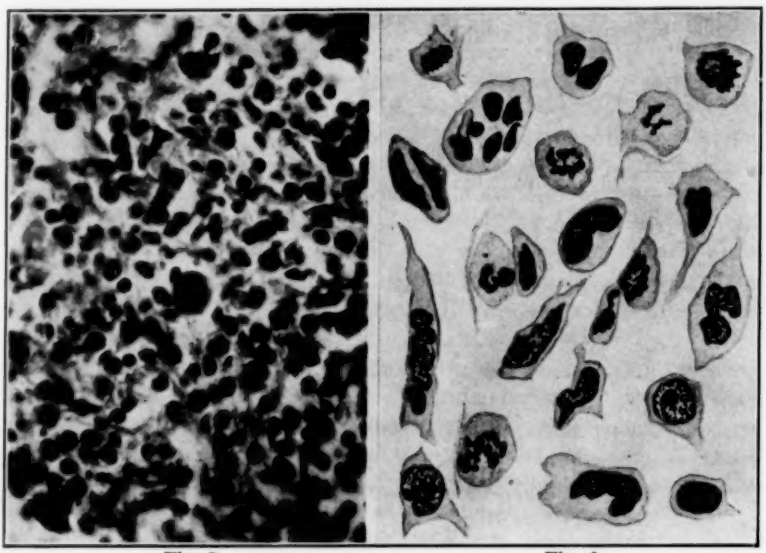

Fig. 5. Fig. 6.

Fig. 5.—Photomicrograph of a section of the mediastinal node removed at autopsy, showing several reticulum giant cells of Sternberg-Reed type, together with dense infiltration of eosinophiles and a few neutrophiles. Some of the granulocytes are premyelocytes and myelocytes. Hematoxylin-eosin (×850).

Fig. 6.—Drawing of some of the typical reticulum giant cells (Sternberg-Reed type) found in the sections of a mediastinal mass. Nuclear configuration of some of the cells suggests mitosis. (Camera lucida, oil immersion lens, 10 ocular; Kingsley's hematologic stain.)

assume from such a viewpoint that eosinophilic infiltration of the lymph glands occurs independently of blood eosinophilia and is consequently not the result of cellular colonization from the bone marrow. Since the eosinophiles are formed in increasing numbers in the lymph glands as well as in the bone marrow, probably by both direct and indirect cell division, these cells finally escape into the blood stream, producing the unique picture presented by this case. While but a hypothesis, this interpretation alone can account for the sequence of

events which seem to have transpired in the pathogenesis of eosinophilic infiltration evidenced first by the lymph nodes and then later by the circulating blood. Irrespective, then, of the nature of the etiologic agent which activates the hemopoietic organs to develop the histopathologic picture found in the present case, it must be assumed that the fundamental pathogenesis in Hodgkin's disease is quite similar to, if not identical with, that of leucemia, an assumption advocated by Warthin (1927), Pullinger (1932), and others.

Another significant histologic feature of the lymph nodes in this case refers to the histogenesis of the reticulum giant cells, known by a great variety of synonyms. Originating from the connective tissue framework forming the bulk of the lymph sinuses in the medulla, these cells are seen to pass through progressive stages of maturation and differentiation, finally attaining enormous dimensions with multilobulated nuclei. These cells are generally regarded as the only specific cellular element which characterizes the Hodgkin's lymph nodes and have been designated as the Hodgkin cell (Potter, 1935). The cytologic characteristics of the Hodgkin cell have been so carefully studied and described by Sternberg (1898), Andrewes (1902), Reed (1902), and others that their detailed description here is superfluous. It is only necessary in this connection to state that the lymph node sections demonstrated the various developmental stages by which the giant cells differentiate and that even a few of these cells presented certain nuclear characteristics strongly suggestive of mitotic division (Fig. 6).

Morphologically the well-differentiated reticulum giant cells are indistinguishable from the megakaryocytes (known also as myeloplaxes or multinuclear myeloid giant cells) of the normal bone marrow, a feature which led Medlar (1931) to regard Hodgkin's disease as a primary neoplastic disease of the bone marrow with the proliferation of the megakaryocytes as the type cells, a pleomorphic aggregation of similar cells in the involved lymph glands being merely metastatic tumor growth. A somewhat similar conception was earlier expressed by Symmers (1924) to the effect that the histogenesis of Hodgkin's disease is determined by the "discharge of mononuclear giant cells from the bone marrow and their arrest by the hyperplastic lymphoid depots in pursuit of their function as filters." Such an assumption, however, would seem unnecessary inasmuch as both mononuclear and multinuclear giant cells can be clearly demonstrated to originate and mature within the lymph nodes themselves. Moreover, such a development occurring in the lymph gland may be looked upon as added indication that myeloid metaplasia rather than metastatic tumor growth constitutes the essential histopathology of Hodgkin's disease, bringing it more in line with the category of leucemias.

Finally, the present case is unique in that the patient belonged to a sickle-cell family, as established by positive tests of his red blood cells. In the sections of the lymph glands removed at biopsy, the small vessels were filled with large clumps of blood in which were found many sickle cells. Although the patient betrayed no active symptoms of sickle-cell anemia, the coexistence of lymphogranuloma and sicklemia offers an interesting opportunity to speculate on the possibility of their having a mutual relationship. Both of these diseases, although so far as is known having nothing in common other than certain aspects of pathologic changes in the spleen, are recognized as having definite hereditary and familial tendencies. No conclusion, however, can be drawn from the observation in a single case.

SUMMARY AND CONCLUSIONS

1. A case of Hodgkin's disease with terminal eosinophilia occurring in a negro child belonging to a sickling family is reported.

2. Eosinophilia in the present case was a terminal phenomenon, totally absent during the early stages of the disease, although the involved lymph node removed at biopsy revealed a marked infiltration with eosinophiles. This naturally leads to a conclusion that the peripheral eosinophilia was the result rather than the cause of tissue eosinophilia. Evidence, therefore, points to the possibility that the eosinophiles infiltrating the affected node are not derived from the similar cells transported from the bone marrow by way of the blood stream, but rather these cells arise in situ as the result of myeloid metaplasia.

3. The multinuclear giant cells, known by numerous synonyms and regarded as absolutely unique in Hodgkin's disease, are cytologically indistinguishable from normal megakaryocytes in the bone marrow and therefore, in all probability, these cells do not constitute a distinct strain of pathologic cells but represent the differentiation of reticulum cells under the influence of some pathologic stimulation. In other words, the development of the multinuclear giant cells takes place in situ in the lymph nodes themselves and their presence is not likely to have resulted from the transportation of these cells from the bone marrow. This interpretation of the pathogenesis of the giant cells in the Hodgkin's nodes adds further evidence as regards the phenomenon of myeloid transformation of lymph glands in this disease.

4. On histologic grounds, then, consisting chiefly of myeloid metaplasia occurring in the lymph nodes, Hodgkin's disease resembles myelogenous leucemia, these two conditions differing in that in leucemia the blood changes are fairly constant whereas in Hodgkin's disease the peripheral blood picture is scarcely altered. Thus, it is suggested that Hodgkin's disease ought to be classed among the diseases of the hemopoietic organs, particularly the lymph nodes and

the bone marrow; the characteristic changes being the disorderly multiplication of granulocytes (both eosinophilic and neutrophilic), megakaryocytes, and lymphocytes, accompanied by a fibroblastic proliferation leading to fibrosis but in which, save for the rare instances in which an increase in circulating eosinophiles during the last stage reflects the underlying pathology of the involved tissue, the peripheral blood shows no leucemic changes.

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SEVERE FUNCTIONAL ANEMIA IN A CHILD, RESEMBLING PERNICIOUS ANEMIA OF ADULTS

A Case Study

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A GENUINE revival of interest in the anemias of infancy and childhood has been in evidence during the past decade. This has apparently been an outgrowth of the fundamental contributions in the general field of hematology made by such investigators as Whipple,[1] Minot,[2] Castle,[3] Cooley,[4] Hart,[5] and their coworkers. Because of the natural physiologic lability of the immature subject and the excessive demands of rapid somatic growth, the young child is peculiarly susceptible to those disturbances in nutrition or general metabolism which are thought to favor the development of certain types of anemia. Reasoning along this line, one might expect the incidence of pernicious anemia to be exceptionally high in early life, but such is not the case. In fact, this particular form of anemia is thought to be all but nonexistent before the age of ten years. However, a few authentic reports of its occurrence in older children have been recorded.

The present report deals with an unusual case of "pernicious-like" anemia in a child, who appears to have recovered completely following a course of therapy considered to be more or less specific for genuine pernicious anemia. It is thought worthy of being recorded not merely because of the rarity of this form of anemia in childhood, but more particularly because of the complete and apparently permanent disappearance of all traces of the disorder following a single course of therapy. Almost as important may be the development during convalescence of a bizarre disturbance in the general body metabolism, which suggested a transient malfunctioning of the pituitary or the adrenal gland.

REVIEW OF CASE

E. S., a twelve-year-old girl, was admitted to the pediatric service of the University of Minnesota Hospital on Dec. 12, 1935 with the complaint of pallor, weakness, loss of appetite, and vomiting. She had been considered to be quite well up to three weeks prior to admission, at which time she had had an acute upper respiratory infection with a cough, which still persisted. Weakness, pallor, and listlessness had become marked about ten days prior to admission, and morning vomiting had occurred repeatedly without regard to meals or activity. Slight numb-

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ness and tingling of the hands were complained of on several occasions. Soreness of the tongue and buccal membranes was fairly marked. There was no history of blood loss or purpura or of poisoning of any kind. The diet could not be described with a high degree of accuracy, but the appetite had been noticeably poor and capricious for some time, according to the mother's account. Except for the frequent vomiting and this disturbance of the appetite, there were no gastrointestinal symptoms. There was no special suggestion of iron deficiency in the diet. No members of the immediate family had suffered from anemia or any similar illness. It is worthy of mention, however, that two first cousins have been treated for hemophilia in our clinic.

Physical Examination on Admission.—The patient was a well-developed but somewhat undernourished girl. Her weight was 26.5 kilograms. She was intelligent and cooperative. The temperature, pulse, and respiration were normal. The tongue was completely denuded of papillae and presented a "beefy red," slightly furrowed appearance. Pallor of the skin and mucous membranes was marked. No definite jaundice or purpuric spots were discernible, although a single small hemorrhagic area could be seen in the left conjunctival fold. The lymph nodes of the neck were slightly enlarged. The chest examination was negative except for a soft blowing systolic murmur heard over the precordium. No masses were palpable in the abdomen. The spleen, liver, and kidneys were not demonstrably enlarged. A complete neurologic examination was essentially negative.

Laboratory Data on Admission.—Hemoglobin 22 per cent (Sahli), 3.5 gm. per 100 c.c. of blood (Haden); red blood cells 1,100,000 per c. mm.; white blood cells 4,900 per c. mm. with a normal differential count; platelets 190,000 per c. mm.; reticulocytes 0.3 per cent. The blood smear showed some basket cells, an occasional megakaryocyte, and immaturity in the lymphocytes. Among the polymorphonuclear cells were many band forms. The red cells showed marked anisocytosis and poikilocytosis, with a tendency to macrocytosis. Smears kindly examined for us by Dr. Hal Downey and Dr. O. P. Jones of the Division of Hematology showed "no evidence of leukemia but a severe degree of toxic anemia, the smear suggesting a 'pernicious type' of anemia with numerous 'P.A.' neutrophils." The bleeding time and clotting time were normal. The Wassermann, Kahn, tuberculin, and Shick tests were all negative. No blood or parasites could be found in the stools. The van den Bergh reaction was indirect. Urobilinogen was found to be present in the urine in traces, and the feces contained 104 mg. per day, a normal amount according to Watson.[6] The sedimentation rate was 45 mm. in one hour. Urine examination was entirely negative. Serum calcium was 9.1 and phosphorus 5.1 mg. per 100 c.c. Gastric analyses showed the absence of free hydrochloric acid after test meals and after histamine administration (Fig. 1).

Clinical Course.—During the first two days after admission to the hospital, the patient ran an afebrile course without complaints other than those already referred to. On the third day, however, her temperature rose to 101° F. and remained elevated off and on during the following five weeks. The pulse rate remained exceptionally rapid during this period. She coughed occasionally, bringing up a small amount of mucopurulent material. Roentgenograms showed increased bronchial markings in the lower lung fields, suggesting early bronchiectasis. During the first three weeks no other cause for the fever was found although numerous examinations of various types were made. Blood cultures and serum agglutination tests for *B. typhosis, B. paratyphosis* A and B, *B. melitensis, B. tularense,* and *B. dysenteriae,* Flexner and Shiga, were all negative.

Following the preliminary diagnostic studies, the patient was given a transfusion of 500 c.c. of blood on December 23. The response to this and to a second transfusion of 525 c.c. four days later was only transitory so far as the blood picture was concerned. The hemoglobin rose from 22 to 37 per cent but again fell within a few days to 19 per cent. The patient still complained of sore tongue, especially when eating. Gastric analysis at this time (January 2) again revealed the absence of free hydrochloric acid.

Because of the pernicious-anemia-like picture, she was given liver extract (anti-pernicious-anemia factor—Lederle) intramuscularly in 6 c.c. doses on January 10 and January 18. The temperature gradually fell to normal following the first injection. As shown graphically in Fig. 1 the response to these injections was spectacular, particularly as regards the reticulocyte count. It is obvious that the mechanisms involved in hemoglobin and red blood cell regeneration were stimulated almost to their maximal capacity. Gastric analyses made on several occasions after the blood picture had returned to normal showed free hydrochloric acid, as indicated in Fig. 1.

The patient's temperature remained normal or but slightly elevated until January 29, at which time it again rose to 103.4° F. For the first time the patient complained of pain in her left thigh, and the next day showed signs of thrombophlebitis. On the following day similar symptoms and signs appeared over the right thigh also. Redness, swelling, and edema were present with acute tenderness over the saphenous vein. The abdomen was distended, and the superficial veins became somewhat prominent. During the course of this sharp febrile reaction, the reticulocyte count dropped from its maximal elevation of 21.0 per cent to 0.8 per cent. On January 31 a third dose of liver extract was administered. After approximately ten days of septic fever, the body temperature again began to decline, coincidently with subsidence of the

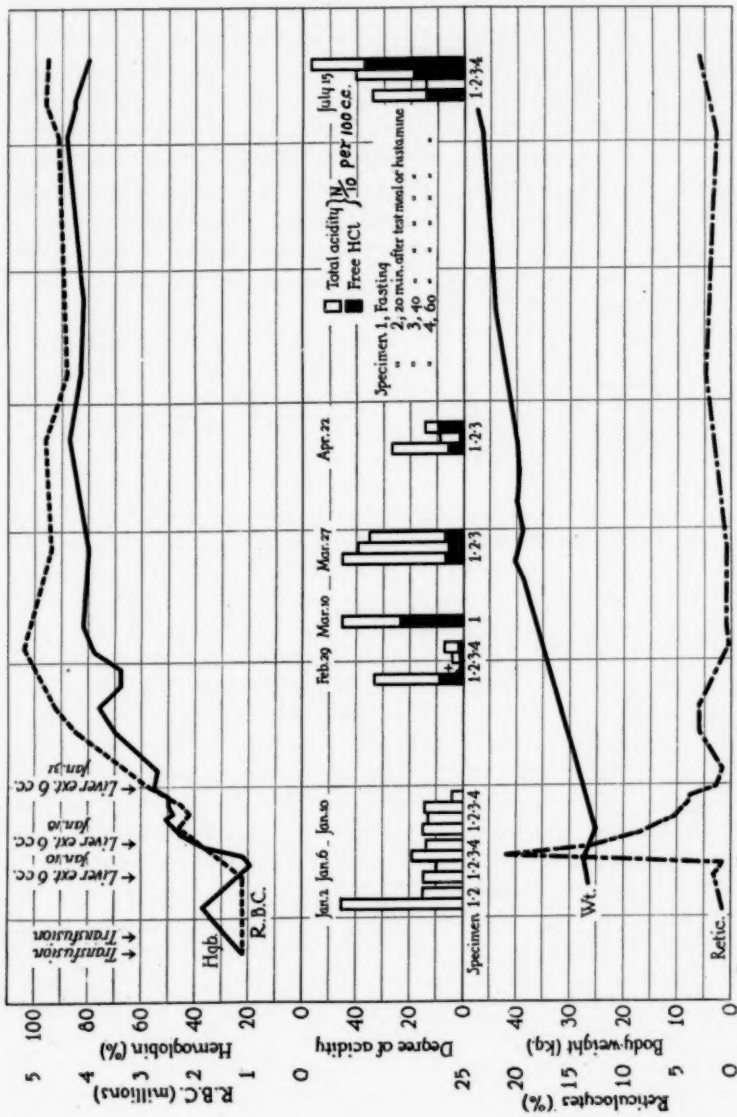

Fig. 1.—Graphic representation of changes in the blood picture, gastric acidity, and body weight as a result of liver therapy.

thrombophlebitis. The reticulocyte count shortly thereafter rose spontaneously to 3.0 per cent. Within a month following institution of liver therapy, the blood picture had become entirely normal and remained so thereafter. The gastric juice continued to contain free hydrochloric acid.

To insure a complete and satisfactory convalescence, particularly in respect to the complicating thrombophlebitis, the patient was kept in the hospital for three months following subsidence of the acute infectious process. Her appetite, which had become excessive following the liver therapy, continued and the weight change was marked, representing a gain from 26 to 47 kilograms (Fig. 1). In spite of a moderate reduction in her diet, she continued to gain and complained of hunger almost continuously. In an attempt to discover the cause of her polyphagia and obesity, the carbohydrate tolerance and the basal metabolic rate were determined. The latter was found to be low on two occasions (minus 38 per cent and minus 29 per cent). Fasting blood sugar values ranged between 89 and 110 mg. per 100 c.c. The glucose tolerance test showed the following values: fasting, 89; 1 hour, 133; two hours, 122 and three hours, 106 mg. per 100 c.c. of blood. A moderate grade of acrocyanosis of the upper as well as the lower extremities gradually developed. At this time the hemoglobin ranged near the 100 per cent level, while the red blood cell count was found to be slightly above 5,000,000 on one occasion. At the same time her face became full, pudgy, and suffused. The fat was deposited chiefly over the torso, face, and neck with purplish striae formation over the abdomen and hips. X-ray pictures of the hip and the long bones showed a moderate degree of osteoporosis. These changes were sufficiently striking to suggest the adrenal cortical syndrome or Cushing's "pituitary basophilism" in an early stage. The blood pressure, however, varied between 102/58 and 108/78 only. A roentgenogram of the sella turcica was negative and no mass could be palpated in the slightly distended abdomen. She was discharged from the hospital on July 15, 1936 with this syndrome representing her only recognizable abnormality.

Since that time the patient has been examined periodically in the out-patient department. The above signs suggestive of an endocrinopathy, involving the pituitary or the adrenal cortex, have all disappeared completely. She has had no recurrence of the anemia. The blood count on June 3, 1937 was as follows: hemoglobin, 90 per cent; red blood cells, 4,710,000 per c.mm.; total white blood cells, 5,980 per c.mm.; polymorphonuclears 62 per cent; lymphocytes, 36 per cent; and monocytes, 2 per cent. No therapy has been required during the past year and there have been no symptoms or signs of illness, whatsoever. So far as can be determined at the present time, she is a normal child in every respect.

COMMENT

This case study is of interest primarily because it demonstrates the occurrence of a type of anemia in childhood, which resembles pernicious anemia of the adult type very closely even though proof of their identity is lacking. The fact that our patient completely recovered following specific therapy, together with lack of direct information regarding the presence or absence of the intrinsic antianemic factor in the gastric contents, makes a positive diagnosis of true pernicious anemia unjustifiable. As pointed out by Castle, Heath and, Strauss[3-b] the absence of free hydrochloric acid in the gastric contents does not necessarily indicate the lack of the essential intrinsic factor. Nor does return of free acid imply return of the intrinsic substance, when both have previously been demonstrated to be absent. Unfortunately special tests for the intrinsic factor could not be carried out in the present case. If any diagnostic significance can be attached to her response to specific therapy, however, it must be admitted that she probably suffered temporarily from a lack of this essential factor.

The underlying pathogenesis of the anemia in this particular case is obscure. Whether or not the vomiting was a contributing factor on the basis of loss of intrinsic substance or was merely an associated symptom dependent upon an underlying disturbance in gastric function could not be determined. Since the onset of the patient's anemia was preceded by an acute febrile illness, it seems to us that the latter may have been responsible for a transient functional disturbance of the mechanisms normally responsible for the production of both free hydrochloric acid and the intrinsic antianemic factor. The patient's striking response to parenteral administration of the latter substance and her subsequent course indicate that the deficiency was thereby corrected temporarily, after which normal function was completely restored.

Whether development of the profound disturbance in body metabolism noted following recovery from the anemia bears any relationship to the response of the hematopoietic system or not is problematic. We have been unable to find any reference to such an interrelationship in the literature. While there is some evidence which points to an intermediary effect of the anterior pituitary on hematopoiesis,[7] insufficient data are available for a satisfactory interpretation in the present case. The clinical picture suggestive of mild "pituitary basophilism" or the "adrenal cortical syndrome" developed on what was apparently a purely functional basis, since it disappeared spontaneously and completely within less than a year.

SUMMARY

1. A case of severe anemia, closely resembling pernicious anemia of adults, is described as occurring in a twelve-year-old child.

2. Parenteral administration of liver extract (antipernicious-anemia factor) was followed by a spectacular recovery, which was apparently complete and permanent.

3. This was interpreted tentatively as representing a transient, purely functional disturbance in the mechanism involved in the elaboration and utilization of the intrinsic antianemic factor.

4. A bizarre sequela in the form of a temporary abnormality of body metabolism resembling "pituitary basophilism" or the "adrenal cortical syndrome" is likewise described.

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FREE DIET IN CHILDREN WITH DIABETES

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THOSE with experience in the preinsulin days remember the terrible existence that diabetic children had to sustain. The extremely strict diet supplied to these unfortunate children scarcely contained anything that could appeal to the taste of children in general. In spite of all privation the result of the strict diet always became unfavorable after a very short time. With the introduction of insulin new therapeutic prospects were opened. The new remedy gave us the possibility of supplying a more liberal diet, of meeting the risks of infection with more confidence, and of overcoming the state of coma in a new way.

In my opinion, however, it would have been possible to take at an earlier date the full advantage of the introduction of insulin in therapeutics. Insulin was used in the beginning as an auxiliary to a strict-dietetic treatment, which later was regarded, and is still regarded in many quarters, as the main point. As a result, the fate of children suffering from diabetes, as a rule, has remained most deplorable in spite of the insulin. They have still had to endure, so to speak, a restricted existence. They have not been allowed to enjoy the pleasure of satisfying their hunger in a normal way, and they have still been treated as exceptions, which has been anything but advantageous especially with regard to their psychical development. To this very day many physicians have endeavored to keep the insulin doses down as far as possible, indeed, to try to carry on without insulin at least for some time, even if the diet must be extremely strict.

By degrees the views on this matter have changed. More and more the conclusion has been reached that children suffering from diabetes should be allowed to lead as normal a life as possible. Kirsten Utheim-Toverud, for instance, emphasized in 1931 the advantage of diabetic children's being allowed to share the food of their brothers and sisters, an advantage "which can hardly be overestimated in connection with a disease lasting for life." A similar point of view has been expressed by Friderichsen in his book on diet in 1933, in which he states: "Psychologically it is better to accommodate the doses of insulin to the food than vice versa."

The first who seems to have gone in deliberately for a quite free diet in connection with diabetes of children was Stolte, of Breslau, whose results published in 1931 seemed to be very favorable in a number of cases. In 1934 Söderling gave an account of some good results with similar treatment.

From the Pediatric University Clinic Kronprinsessan Lovisas Vardanstalt, Stockholm, Director A. Lichtenstein.

I personally have been using free diet for more than four years and in my teaching have consistently emphasized the importance of letting the diabetic child have a chance of living a normal life with free choice of food, and giving a sufficient quantity of insulin. By *free diet* I mean an absolutely free diet without any restrictions and without weighing the food or any of its ingredients. In other words, the children can fully satisfy their appetite and to some extent their individual taste, i.e., with regard to the supply of nourishment, and live a quite normal life. The only direction I give regarding the diet is to avoid luxury, which also ought to be avoided by healthy children.

The insulin is given in doses sufficient to keep the child in good general condition, in good increase of weight and free from ketone bodies in the urine. On the other hand, I have attached little importance to a somewhat greater or lesser sugar excretion, in case the increase has not appeared in connection with a change for the worse in the general condition of the child or in the weight curve.

Up to the present I have used such treatment in about 50 cases, partly in the Kronprinsessan Lovisas children's hospital and in my private practice. The patients are children from the ages of two and one-half to sixteen years. Most of the cases have been followed for several years, the oldest one for fourteen years and most of the others from two up to eight years. A few cases have been early. All of them are to be considered as grave cases of diabetes in as much as in all of them coma, or threatening coma, has occurred once or repeatedly. The free diet has been carried through for a time varying from one-half to four-five years.

In most cases the children have been admitted to the hospital for the change to a free diet, and consequently I have been able to observe them thoroughly during that period. As a general opinion, I will first state that the change from the restricted to the free diet has always been very easy and has taken place without any disturbances.

It is a matter of course that the patients themselves and their families highly appreciate the release from strict dietary schedules and from the daily trouble of weighing and measuring the allowed quantity of food. But it is necessary to witness the joy of the diabetic children at the release in order to understand fully the psychologic importance of the free diet. The matter has a further importance. One obtains the definite impression that the altered psychologic sense, the release from being placed in an exceptional situation in relation to other children has a direct favorable influence on the disease of the patient.

As a first result of the release from restrictions we find that the children as a rule show signs of *voracious hunger for carbohydrates.* Very soon, however, the child spontaneously passes on to a more normal consumption of carbohydrates which varies but little. In doing so, however, the child always keeps the supply of carbohydrates on a higher level than previously. For instance, a boy of seven years, who had received

about 110 gm. of carbohydrates before being changed over to a free diet, consumed immediately after the change 300 gm. daily. After some time, however, he reduced of his own accord the consumption of carbohydrates to about 200 gm. daily. Instead of a supply of carbohydrates, which during the restricted diet was usually 90-110-130 gm., varying according to the age, the children have generally consumed, when the food is chosen on free impulse, 150-250 gm. daily and sometimes even more.

Any inconvenience on account of the increased supply of carbohydrates has not been observed. On the contrary, the condition of the patient has always been favorably influenced and often to a considerable extent. Even the weight curves have reflected improvement, no doubt depending upon the fact that not only the supply of carbohydrate but also the total supply of calories has, as a rule, increased in connection with the change to free diet. Thus children of from nine to twelve years of age, in which group most of my patients are found, have in connection with completely free diet, consumed from 50 to about 70 calories per kilogram and sometimes more.

It might be expected that the blood sugar level, as well as the carbohydrate excretion, would be increased to a great extent if the doses of insulin were not raised correspondingly. But this has not been the case. It is true that some patients on free diet have required larger quantities of insulin than previously, but the increase has usually been moderate and sometimes quite insignificant. In many cases the dose of insulin has been maintained unchanged without inconvenience, and sometimes it has even been possible to reduce it, in spite of the fact that the supply of carbohydrates has been twice the amount previously given. Similar observations were mentioned for example by L. Emmett Holt in 1933.

The blood sugar level has often proved to be more regular than previously, sometimes a little higher, but sometimes considerably lower, and at the same time more uniform. Nor has the urinary sugar excretion been considerably higher during the free diet, but sometimes remarkably low in proportion to the large supply of carbohydrates.

An inconvenience attached to the free diet seems to be that of the usual insulin generally three injections must be given in twenty-four hours, often in cases in which two injections were sufficient during the restricted diet. Only in rare instances have my patients been able to do with two injections in twenty-four hours in connection with free diet.

It stands to reason that the supply of insulin through injections always becomes stiff and schematic compared with the smooth variations in the production of insulin from a healthy pancreas. On the other hand, three daily injections make it possible to bring about, in the grave cases of diabetes, a better distribution of the insulin than two injections.

Instead of using the usual insulin we have during the last year more and more passed over to the use of Hagedorn's protamine insulin (insulin rétard). This preparation, a combination of insulin and

protamine, is absorbed much more slowly than the usual insulin. On account of this it has been possible to reduce the insulin doses from three to two, and in many cases even to only one injection per day, in spite of keeping the child on a free diet. The treatment of a difficult case of diabetes has been simplified as far as possible at present, when the patient, after having taken his insulin injection in connection with his morning toilet, needs to think no further of his illness until the next morning.

With free diet, at least according to my experience up to the present, the risk of an overdosage of insulin with consequent trouble and inconvenience is far less than with restricted diet. In only one of my patients, a boy with rather varying and sometimes bad appetite, have I observed symptoms of insulin shock in connection with free diet. In all other patients no such symptoms have been traced as yet.

A fact of great interest, and no doubt of great importance, is that the ketonuria disappears, or at least decreases considerably, after the change to free diet. Children, who had earlier always shown decided positive reactions to the Gerhardt and Legal tests and who in many instances had to be admitted to the hospital again and again with threatening or developing coma, have, after being placed on a free diet, been totally or almost totally free from these difficulties.

Further it is manifest that intercurrent infections, which are known to constitute permanent danger for the child suffering from diabetes, after the change to free diet generally have been overcome much more easily, and exert much less influence on the metabolism than is the case with restricted diet. As a consequence we have found that our diabetic children, who earlier were permanently returning guests at the hospital, often several times every year, now almost without exception can be easily cared for outside the hospital.

Although it is not my intention to enter into particulars with regard to case histories, I wish, however, to mention a case which gives, in my opinion, a good illustration of the advantages of the free diet.

A girl aged two and one-half years, whose diabetes had been diagnosed at the age of one and one-half years, was nursed from that time in a hospital for an entire year with strict diet and insulin up to 22 units. During the entire time the general condition was bad with permanent ketonuria and, as a rule, high acetone content. Further, symptoms of urinary infection were present. When taken in at the Kronprinsessan Lovisas Hospital, she was precomatic and showed pyuria and symptoms of infection in the upper respiratory tract with fever.

As soon as the coma had been overcome, she was placed on a free diet. The child consumed 62 calories per kilogram (about 100 gm. of carbohydrates) and received 34 (12 + 10 + 12) units of insulin. She improved rapidly so that the renal affection could be investigated through pyelography. It was found to be due to a stone the size of a hazelnut, which could be removed through pyelotomy. The child went through the operation well and was in condition after five weeks to be discharged on a free diet (about 80 calories per kilogram—70-80 gm. of carbohydrates) with 30 units of insulin (10 + 10 + 10), acetone-free, and with a good increase of weight.

This girl had been attended by a competent doctor in a hospital for an entire year, without her condition ever becoming sufficiently improved so that her renal affection could be investigated. After the change over to the free diet, it was possible, in the course of some weeks, not only to improve her general condition in such a way that pyelography could be tried, but the patient could also be operated upon for the removal of stone in the kidney and very soon be discharged in excellent condition.

As shown above, my experience with a completely free diet in connection with diabetes of children is up to the present very favorable. It is certainly true that the time of observation for some of the cases does not yet amount to a year and, therefore, for a disease such as diabetes, must be regarded as short. But the improvement has always been so obvious and, during months or in many cases up to four to five years, proved to be so permanent that I have found it advisable to make this experience known. My own opinion is that with a really free diet for the first time full advantage has been taken of the introduction of insulin in the therapeutics of diabetes.

THE INFLUENCE OF A DAILY SERVING OF SPINACH OR ITS EQUIVALENT IN OXALIC ACID UPON THE MINERAL UTILIZATION OF CHILDREN

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BECAUSE milk, fruit, and green leafy vegetables contain protein of excellent quality, or a generous and well-balanced mineral mixture, and a supply of vitamins essential for life and well-being, they have been called "protective foods."[1] As might be expected, green leafy vegetables vary in their content of vitamins and minerals depending upon the class and variety, the climate, the soil in which they are grown, and the way they are marketed and handled before consumption. On the other hand, little thought had been given until recently to untoward properties resident in the commonly used foods and their effects upon the organism. It is now known that some of these foods contain toxic substances, such as fluorine,[2] selenium,[2] and oxalic acid,[3] which are toxic when taken into the body in sufficiently large quantities. These substances are not only present in small and variable amounts in foods, but might also be natural constituents of the body.

The realization of a relatively high oxalic acid content in spinach, in contrast to some of the other green leafy vegetables, and the deleterious effect of these amounts of oxalic acid upon calcium metabolism in the rat, has attracted renewed interest in its consequence in the metabolism of man.[4-6] Although spinach has been used as a staple vegetable in the dietary of man, and for years has been placed on the diet list of practically every menu illustrating the adequate dietary for adult, child and infant alike, it is now being scrutinized anew. As a matter of fact, the majority of investigations on the nutritive value of spinach have usually been for a different purpose other than for a study of its deleterious properties in average servings and have included enormous quantities of spinach which are all out of proportion to actual dietetic practice. For instance consideration has been given to the availability of calcium[4-9] and iron[9, 10] in spinach, the influence of its bulk[8-10] and its potential acid-base residue[11] upon metabolism. To date the advantages usually accredited to the green leafy vegetables in general are increased gastrointestinal motility, improved appetite, the addition of vitamins and increased intake of minerals, particularly iron.

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Presented before the Division of Biological Chemistry at the ninety-second meeting of the American Chemical Society at Pittsburgh, Sept. 7-11, 1936.

The purpose of the present investigation has been to observe the influence of a daily serving of 100 grams of puréed spinach or its equivalent in oxalic acid upon the nitrogen, calcium, and phosphorus utilization of preadolescent children.

EXPERIMENTAL PROCEDURE

Subjects.—Ten children, aged five to eight years, were carefully selected because of an excellent health record since early childhood, according to the medical examinations.* Their dietaries were controlled for seven months preceding the study of spinach in order to assure mineral reserves. During this time the subjects had demonstrated that they were good eaters, and were cooperative and happy in their environment. Each child was studied with and without spinach or oxalic acid, thus each child served as his own control.

In a previous publication[12] it was pointed out that in fundamental metabolic studies it is extremely important not only to select the subjects carefully in view of their nutritive condition, but to keep them "happy and interested in their wholesome regularity of personal habits, sleep, work, play, and in their healthful living in a home environment where love, security, and serenity abounded."

Dietary and Metabolic Procedure.—The daily intake of simply prepared common foods† was kept constant in quantity and quality for each child throughout the control and experimental periods except for the addition of 100 grams of canned spinach (puréed to assure complete sampling of plant parts) during the latter periods. Each day for five days immediately following the spinach addition, and with the same basal diet, oxalic acid equal to that determined in the spinach fed, was given together with the calcium (calcium acetate) equivalent of the spinach. The basal diet had been used for a period of years in this laboratory and has been found to be satisfactory for children as indicated by their growth in height, weight, and gains revealed by frequent medical and physical examinations. Moreover, it was sufficient to promote nitrogen and mineral storage. The basal diet contained the equivalent of 90 to 100 U.S.P.X. units of vitamin D and 90 to 120 milligrams of ascorbic acid daily.

The calcium intake of eight of the children approximated 0.8 gram daily while that of the two eight-year-olds was 1.3 grams. The oxalic acid content of the 100 grams of spinach fed amounted to 0.7 gram. The calcium contributed by the spinach supplement represented only 5 to 7 per cent of the total intake. Since the free oxalic acid of the spinach will combine with the calcium of the other foods eaten simultaneously, any untoward effect on calcium retention will depend upon the quantity of spinach consumed and the adequacy of the calcium in the diet.

*Marsh W. Poole, M.D., pediatrician at the Children's Village, not only attended the children during the present study and made all the medical and physical examinations but he had followed them at regular and frequent intervals for several preceding years.

The skeletal structure and maturity of the children were kindly evaluated by T. Wingate Todd, M.D., and C. C. Francis, M.D., of Western Reserve University, Cleveland, according to their highly specialized and standardized x-ray technique and interpretation.

†List of common foods used in the basal diet:

Apple
Banana
Lean beef
White and whole wheat bread
Butter fat
Cabbage
Carrots
Cheese
Corn flakes
Egg
Graham crackers
Lettuce
Milk
Orange juice
Peanut butter
Potato
Shredded wheat
Sugar
Tomato juice

TABLE I

AVERAGE DAILY CALCIUM, PHOSPHORUS, AND NITROGEN RETENTION DURING CONSUMPTION OF A CONTROL DIET, WITH A SUPPLEMENT OF 100 GRAMS OF PURÉED SPINACH OR ITS OXALIC ACID EQUIVALENT (GRAMS PER DAY)

CHILD	DIETARY	AGE* MO./DAY	HEIGHT* (CM.)	WEIGHT* (KG.)	OBSERVATION DAYS	CALCIUM				PHOSPHORUS				NITROGEN			
						INTAKE	URINE	FECES	BALANCE	INTAKE	URINE	FECES	BALANCE	INTAKE	URINE	FECES	BALANCE
F. C. (M)	Control I	82/12	119.4	22.8	25	0.768	0.062	0.567	0.140	1.107	0.587	0.438	0.082	10.49	9.06	1.11	0.33
	Spinach	83/ 8	119.8	23.2	15	0.830	0.069	0.592	0.170	1.202	0.635	0.423	0.144	10.85	9.49	1.08	0.28
	Oxalic acid	83/23	119.8	23.4	5	0.837	0.054	0.640	0.143	1.122	0.594	0.453	0.075	10.56	8.71	1.03	0.82
	Control II	83/28	119.8	23.4	15	0.775	0.068	0.549	0.157	1.095	0.570	0.438	0.086	10.45	8.73	0.99	0.73
H. H. (M)	Control I	88/ 0	119.4	21.2	25	0.768	0.046	0.616	0.107	1.107	0.537	0.509	0.062	10.49	9.02	1.30	0.18
	Spinach	88/25	119.7	21.4	15	0.830	0.048	0.635	0.147	1.202	0.555	0.483	0.164	10.85	9.03	1.32	0.50
	Oxalic acid	89/11	119.9	21.5	5	0.837	0.042	0.661	0.134	1.122	0.572	0.446	0.104	10.56	8.39	1.19	0.98
	Control II	89/16	120.0	21.4	15	0.775	0.049	0.612	0.115	1.095	0.554	0.490	0.051	10.45	8.91	1.21	0.34
P. W. (F)	Control I	80/ 6	117.4	23.0	25	0.768	0.071	0.522	0.175	1.107	0.679	0.290	0.137	10.49	8.37	1.16	0.95
	†Spinach	81/ 2	117.9	23.6	10	0.830	0.076	0.552	0.202	1.202	0.726	0.320	0.157	10.85	8.70	1.16	1.00
	†Control II	81/27	118.6	23.4	10	0.775	0.069	0.526	0.180	1.095	0.630	0.282	0.184	10.45	7.88	1.22	1.34
J. M. (F)	Control I	77/ 6	116.3	21.5	25	0.753	0.077	0.530	0.146	1.032	0.618	0.280	0.134	10.02	8.40	0.98	0.65
	Spinach	78/ 2	116.5	22.1	15	0.825	0.079	0.583	0.163	1.175	0.697	0.338	0.140	10.74	8.94	1.05	0.75
	Oxalic acid	78/17	116.8	22.3	5	0.832	0.066	0.582	0.184	1.095	0.738	0.293	0.064	10.45	8.68	0.90	0.87
	Control II	78/22	116.8	22.3	15	0.775	0.070	0.521	0.184	1.095	0.657	0.332	0.106	10.45	8.55	1.00	0.90
B. F. (F)	Control I	71/15	110.2	19.3	25	0.753	0.062	0.568	0.123	1.032	0.641	0.298	0.093	10.02	8.34	1.09	0.59
	Spinach	72/10	110.7	19.7	15	0.825	0.054	0.610	0.161	1.175	0.678	0.356	0.141	10.74	8.82	1.11	0.80
	Oxalic acid	72/25	110.7	19.9	5	0.832	0.047	0.615	0.170	1.095	0.807	0.316	0.028	10.45	8.61	1.08	0.76
	Control II	72/30	110.7	20.0	15	0.775	0.053	0.520	0.202	1.095	0.653	0.316	0.126	10.45	8.45	1.05	0.95

TABLE I—CONT'D

CHILD	DIETARY	AGE* MO./DAY	HEIGHT* (CM.)	WEIGHT* (KG.)	OBSERVATION DAYS	CALCIUM				PHOSPHORUS				NITROGEN			
						INTAKE	URINE	FECES	BALANCE	INTAKE	URINE	FECES	BALANCE	INTAKE	URINE	FECES	BALANCE
J. H.	Control I	59/25	107.0	18.4	25	0.804	0.102	0.524	0.178	1.122	0.720	0.296	0.106	10.12	8.12	1.17	0.84
(M)	Spinach	60/19	107.5	18.7	15	0.825	0.123	0.526	0.176	1.175	0.749	0.337	0.089	10.74	8.96	1.20	0.58
	Oxalic acid	61/ 5	107.6	18.7	5	0.832	0.115	0.541	0.176	1.095	0.755	0.287	0.053	10.45	8.45	1.09	0.91
	Control II	61/10	107.7	18.7	15	0.775	0.138	0.467	0.170	1.095	0.715	0.295	0.085	10.45	8.38	1.05	1.02
B. M.	Control I	67/11	106.0	17.8	25	0.774	0.070	0.528	0.176	1.029	0.693	0.269	0.067	9.32	7.75	0.97	0.61
(F)	Spinach	68/ 5	106.4	18.4	15	0.783	0.094	0.559	0.131	1.026	0.680	0.302	0.044	9.73	8.25	1.00	0.48
	Oxalic acid	68/20	106.7	18.5	5	0.792	0.089	0.548	0.155	1.008	0.710	0.249	0.049	9.44	8.17	0.82	0.45
	Control II	68/25	106.7	18.6	15	0.733	0.097	0.483	0.153	1.008	0.660	0.263	0.085	9.44	8.09	0.88	0.47
R. S.	Control I	69/20	114.8	19.4	20	0.804	0.102	0.604	0.098	1.122	0.696	0.314	0.112	10.12	8.08	1.25	0.78
(M)	Spinach	70/16	115.2	19.8	15	0.825	0.100	0.602	0.123	1.175	0.728	0.355	0.091	10.74	8.78	1.21	0.75
	Oxalic acid	71/ 0	115.4	19.8	5	0.832	0.051	0.645	0.136	1.095	0.766	0.330	0.010	10.45	8.86	1.11	0.48
	Control II	71/ 5	115.6	19.8	15	0.775	0.080	0.532	0.163	1.095	0.668	0.316	0.111	10.45	8.24	1.05	1.16
W. P.	Control I	99/17	118.7	24.5	25	1.259	0.082	1.029	0.148	1.491	0.886	0.465	0.140	12.34	10.22	1.23	0.89
(M)	Spinach	100/13	119.1	24.8	15	1.317	0.077	1.068	0.172	1.583	0.923	0.461	0.199	12.70	10.42	1.26	1.02
	Oxalic acid	100/27	119.5	25.0	5	1.324	0.066	1.075	0.183	1.503	0.980	0.363	0.160	12.41	10.05	1.18	1.18
	Control II	101/ 1	119.6	25.1	15	1.267	0.079	0.991	0.197	1.503	0.897	0.467	0.139	12.41	10.10	1.05	1.26
D. P.	Control I	102/ 3	136.3	27.7	25	1.259	0.138	0.946	0.175	1.491	0.843	0.440	0.208	12.34	11.07	1.06	0.21
(M)	Spinach	102/22	136.4	27.9	40	1.314	0.138	1.002	0.174	1.547	0.952	0.436	0.159	12.66	10.90	1.33	0.43
	Oxalic acid	104/ 8	136.9	28.6	5	1.324	0.150	1.025	0.149	1.503	1.070	0.334	0.099	12.41	11.04	0.98	0.39
	Control II	104/13	137.0	28.4	15	1.267	0.138	0.978	0.151	1.503	0.937	0.451	0.115	12.41	10.73	1.19	0.49

*Age, height, and weight are given for beginning of dietary regimen.
†P. W. was removed from study during three periods.

The food, urine, and feces were collected quantitatively and analyzed for nitrogen,[13] calcium,[14] and phosphorus[15, 16] in successive five-day balance periods.*

RESULTS AND DISCUSSION

One hundred and twenty-one five-day metabolic balances (605 days) for each of nitrogen, calcium, and phosphorus have been made on ten growing children and are presented in Table I. The individual physiologic response characteristic for each child has been determined for sixty successive days on eight children and for forty-five days on one child. During the initial period of twenty-five days the children consumed the basal diet which was immediately followed by fifteen days on the control diet with a supplement of 100 grams of spinach daily, then five days on the same diet in which oxalic acid and calcium were substituted for their equivalents in 100 grams of spinach daily, and finally fifteen days on the basal diet. The tenth child, an eight-year-old boy, D. P., was observed for a period of eighty-five consecutive days, the first twenty-five days of which he received the constant controlled food intake which was followed by forty days with a dietary supplement of 100 grams of spinach daily, five days with oxalic acid and calcium substituted for the spinach and lastly fifteen days on the control diet.

The average daily amounts of nitrogen, calcium, and phosphorus ingested and excreted in the urine and feces, from which the quantity retained per day for each child is determined, during the successive dietary regimens are recorded in Table I. The storage rates of these elements were not significantly altered by the daily addition of 100 grams of spinach, and moreover, they are compatible with the normal variations of these elements observed in growth. The differences between the average daily storage for the initial twenty-five-day control period and the fifteen to forty-five days on spinach ranged from –0.26 to +0.32 with an average difference of +0.06 gram of nitrogen, –0.045 to +0.040 with an average of +0.015 gram of calcium, and –0.049 to +0.102 with an average of +0.019 gram of phosphorus for the ten children. Furthermore, the daily substitution of the oxalic acid and calcium equivalent of 100 grams of spinach gave variable results but ones that cannot be interpreted as indicating a deleterious effect. Since this amount of oxalic acid was distasteful, and the results were more academic than practical, only one five-day balance period was secured. From a practical consideration in dietetic management spinach would be fed less frequently, certainly not every day in so generous a serving. From these results, spinach cannot be considered harmful to children of this age group, even in daily servings of 100 grams. This conclusion is further verified by the fact that no cumulative toxic or untoward

*The metabolic balances for magnesium, potassium, sodium, chlorine, sulfur, and iron will be reported at a later date.

effects could be detected in the average daily nitrogen, calcium, and phosphorus assimilation during the periods of spinach or oxalic acid consumption, nor during the control periods immediately following. Furthermore, no deleterious effects were revealed in a large number of other types of physical, chemical, and physiologic measurements.

In this study of the physiologic effect of a daily serving of 100 grams of spinach upon the utilization of nitrogen, calcium, and phosphorus, the

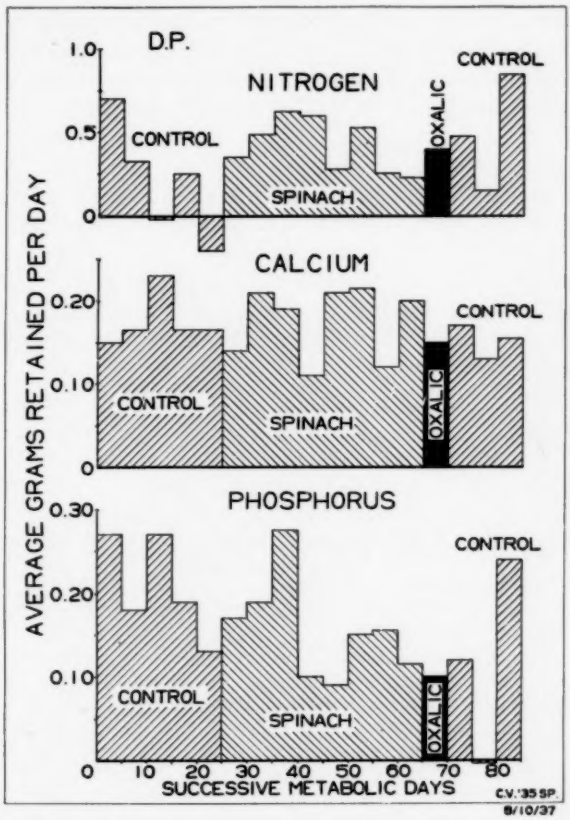

Chart 1.—The increments and decrements of storage of nitrogen, calcium, and phosphorus of an eight-year-old boy during a period of eighty-five days, a part of which included observations on a control diet alone, or with a supplement of 100 grams of spinach daily or its oxalic acid equivalent.

spinach was superimposed upon a diet which had promoted good growth and storage in these same children for several months immediately preceding. The plan herein adhered to was different from those of other investigators who observed the relative availability of the calcium present in spinach as compared with that in milk[4, 6] and over shorter periods

of time. As a matter of fact, green leafy vegetables are not given as a source of calcium, but for other nutritive purposes such as for iron,[9, 10] vitamins,[1] acid-base mineral mixture,[11] or even bulk.[8-10]

Because each child has an individual physiologic growth performance which varies from time to time as maturation proceeds,[17] it is essential in biologic assay of foods to have adequate test periods.[12] Chart 1 shows the increments and decrements of storage of nitrogen, calcium, and phosphorus that may be observed in healthy growing individuals maintained under strict metabolic conditions provided they are followed continuously over a considerable period of time. D. P., an eight-year-old boy, demonstrates the inconsistency of chemical growth and the average daily storage rates characteristic of childhood and illustrates why "it is neces-

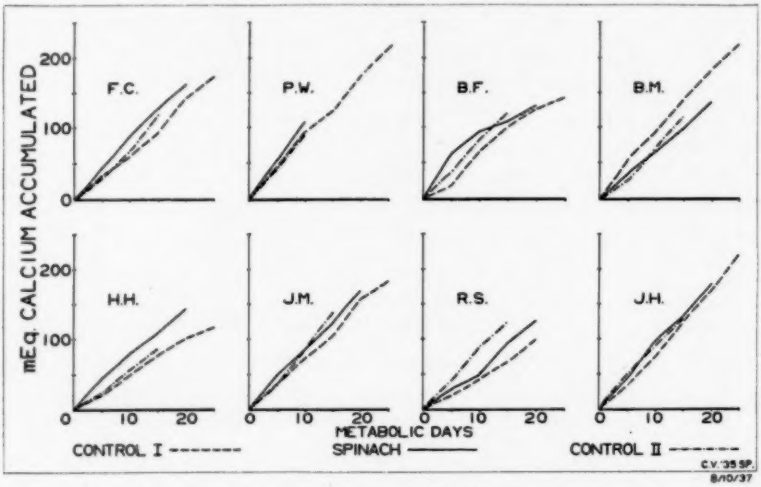

Chart 2.—The cumulative calcium balances for eight children for the initial control dietary, for the spinach, and the final control regimens.

sary to learn throughout a pre-experimental period of several weeks how wide these customary individual rates of storage under highly standardized and desirable conditions before the effect of any regimen upon the metabolic balance can be satisfactorily understood. Without the inclusion of such controlled data one may be easily misled into false fields of interpretation by the use of this method for determining the subsequent effect of certain foods or other factors on metabolism."[12]

Cumulative Storage.—Since the duration of the experimental observations of this investigation extended over sixty to eighty-five continuous days, a new type of interpretation has been permitted which is particularly significant in the consideration of physiologic adjustments that may occur coincident with a change in dietary regimen and, most important, in case of a possible toxicity, an opportunity is given to record

its cumulative effect upon metabolism, i.e., the progressive gain or loss of a particular element over a period of time. The cumulative interpretation of metabolic data shows the progress of growth and any variation therefrom. In addition, it indicates the immediate effect of a dietary shift as well as the gradual metabolic adjustments that a change in dietary regimen may promote. This is illustrated in the cumulative calcium balances for eight of the children for the initial control regimen, for the spinach, and for the final control period as given in Chart 2. Average daily balance data may mask the alterations in rate of storage of an element (Table I). Spinach neither changed the rate of storage of calcium during the twenty- to forty-day period of its consumption now showed a deleterious after-effect during the subsequent fifteen-day control period.

Effect of Spinach on Fecal Outgo.—Although the dry weights of the feces were higher during the ingestion of 100 grams of spinach daily than during the control and oxalic acid periods, there was no consistent increase in calcium outgo in relation to fecal mass. Furthermore, the increased bulk due to the spinach did not accelerate gastrointestinal motility as measured by frequency of defecation, time of appearance of marker, or the wet weight of the feces.

SUMMARY

1. One hundred and twenty-one metabolic balances for each nitrogen, calcium, and phosphorus have been made on ten growing children. The individual physiologic response characteristic for each child on the different dietary regimens has been determined for sixty to eighty-five successive days by five-day balance periods. Each child served as his own control.

2. Control periods of twenty-five days on the ordinary mixed diet of common foods showed the children to be storing nitrogen, calcium, and phosphorus. The storage rates of these elements were not significantly altered by the daily consumption of 100 grams of spinach; moreover, they were compatible with normal variations observed in growth.

3. No cumulative toxic or untoward effects could be determined either in the average daily retentions, or in the progressive storage curves of nitrogen, calcium, and phosphorus either during the period of consumption of spinach and oxalic acid or during the control period immediately following.

4. The supplementation of an already adequate diet with a generous serving of spinach daily, even for as long as forty consecutive days, did not change the rate of calcium storage in growing children when their calcium intake was adequate to cover the precipitating effect of the oxalic acid and provide for their fluctuating growth needs.

5. The practical conclusion drawn from the data recorded herein is that spinach is not harmful even in servings of 100 grams daily, at least

in preadolescent children, but because of its richness in vitamins, minerals, especially iron, and other nutritive essentials it should retain its customary place along with other green leafy vegetables.

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TOXIC ENCEPHALOPATHY IN A CHILD FOLLOWING THE INTERNAL ADMINISTRATION OF POTASSIUM CHLORATE AND SULPHARSPHENAMINE

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UNDER certain circumstances it is justifiable to use toxic drugs therapeutically. There are relatively mild conditions, however, in which such measures are employed at times by physicians in their zeal to "do something." One of these conditions is ulcerative stomatitis caused by the Vincent's organism in which oxidizing agents are usually employed. Of these sodium perborate, hydrogen peroxide, and potassium chlorate are frequently used. In addition spirachetieidal drugs such as the arsphenamines have been used both locally and internally. As a general rule this type of stomatitis is readily amenable to therapy and heroic measures are seldom necessary. For this reason a case is here reported in which severe toxic symptoms followed the use of potassium chlorate and sulpharsphenamine.

B. G., a four-year-old white child, was seen the evening of September 19 with the complaint of repeated vomiting and muscular weakness since that morning. Ten days previously the child had developed a sore mouth which was diagnosed as trench mouth by a physician who prescribed a solution to be applied with swabs and gave the child 0.2 gm. sulpharsphenamine intramuscularly. The latter medication was repeated three days later and at that time, because the child would not cooperate with the swabbings, a saturated solution of potassium chlorate was prescribed to be administered internally in teaspoonful doses every three hours. This latter medication was continued for an entire week. For several days prior to the onset of vomiting the child had taken very little food but had been up and about the house as usual. On the morning of the nineteenth the child began to vomit and emesis continued repeatedly throughout the day, consisting first of curdled milk but soon becoming green. About 10 A.M. difficulty in walking appeared, the gait became staggering, weakness progressed until the child remained in bed and would not even assume a sitting position. A brother, aged six years, also developed a sore mouth which was called trench mouth and received similar treatment with the exception of the internal administration of potassium chlorate.

B. had been a premature infant weighing 3 pounds at birth and 18 pounds at the end of the first year. Development was normal. In 1935 she had had an uncomplicated scarlet fever. A tonsillectomy had been done in August, 1936. The past history was otherwise negative.

The initial physical examination revealed a rather thin, pale, child who was conscious but appeared somewhat disoriented. She was very irritable and resisted examination especially of the mouth. Both upper extremities showed definite paucity of movements and were maintained in a semiflexed position

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with the elbows flexed and the hands partially flexed. Though tonus was good the extremities did not react normally, there being no defense movements and no attempt at grasping objects. The legs showed no paralyses; tendon reflexes were present and hyperactive; there were no pathologic reflexes. There was definite head drop and weakness of the muscles of the back, the patient slumping on attempting a sitting position. There was no rigidity of the neck or back and no abnormalities of sensation could be determined. The pupillary reflexes and ocular movements were normal. There were a few scattered aphthae on the buccal mucosa but no true ulcerative or gangrenous lesions. Examination otherwise was negative.

At this time an atypical poliomyelitis was suspected but the possibility of a potassium chlorate poisoning was also entertained. The child was taken to the Michael Reese Hospital for spinal puncture and further observation and treatment. The spinal fluid was water clear under normal pressure, tests for globulin were negative, and there were ten lymphocytes present. This finding excluded poliomyelitis and the diagnosis of probable potassium chlorate poisoning was made. Blood and urine samples were taken for methemoglobin and the child was placed on continuous intravenous drip therapy with 10 per cent glucose in normal saline.

Her subsequent course in the hospital pointed to severe central nervous system involvement. The child was stuporous, did not talk or swallow, nor did she seem to recognize her mother. On September 21 periodic short convulsive spasms appeared. The pupils dilated, the eyes deviated to the right and clonic twitchings of the face and extremities occurred repeatedly at short intervals. Chvostek's sign was present and there was typical carpal spasm. Head drop was still present but there were no definite paralyses. Calcium gluconate, 15 grains intravenously twice daily, and calcium bromide, 10 grains three times daily by mouth, were administered. That evening there was little improvement, and the twitchings continued. An intravenous transfusion of 160 c.c. whole blood was given and the drip clysis of normal saline and 5 per cent glucose continued. The following morning she was much quieter. Chvostek and Trousseau's signs were negative, her neck was not rigid. The face appeared slightly edematous and distinctly dusky. She was in a deep stupor and would swallow nothing. Feeding by gavage was instituted. On this date the urine was distinctly pink in color, yielded a 4+ benzidine reaction but contained no red corpuscles.

From this time on (Sept. 23, 1936) the child slowly improved. She continued semistuporous, did not recognize her mother or father, but did seem to recognize nurses and doctors and resist their attempts to examine or treat her with violent struggling and screaming. She made no attempts to speak and was entirely unable to swallow. Tube feedings, however, were carried out successfully and the intravenous clysis was discontinued. The eyegrounds were normal at all times.

On Sept. 27, 1936, spinal puncture was repeated. Fluid was water clear and normal except for a colloidal gold curve up to four in the midfield. On this date she was examined by Dr. Roy Grinker who noticed an athetosis of both upper extremities, slight spasticity of the left arm and a + left Chaddock sign. Otherwise there were no findings. He felt the condition was in the nature of an encephalitis with the lesion predominantly in the basal ganglia, the etiology in his opinion being arsenical from the sulpharsphenamine.

From this time the child seemed quieter but still did not recognize or respond to relatives and could not swallow or sit up. October 3 another spinal puncture was done. Fluid was clear, under normal pressure, Pandy was definitely positive,

there was no increase in cells and sugar was 68 mg. per cent. On October 4 the child attempted to swallow for the first time, seemed to recognize her mother and smiled occasionally. She was also able to sit up alone.

October 10 she was examined by Dr. Lewis J. Pollock in consultation. He considered the case a pseudobulbar type of encephalitis, bilateral and deep seated, etiology toxic; but he did not feel it was arsenical since it did not resemble arsenical cases in his experience. Whether potassium chlorate was responsible he felt could not be proved or disproved.

From this time improvement continued very slowly. By Oct. 12, 1936, she was swallowing much better. On October 22 she was much brighter, swallowed well and said "No, No" and "Ouch," her first distinct words. She was able to stand and walk, but still could not use her fingers or hands well and showed her "rage reactions." The following day she was discharged from the hospital.

Laboratory findings while in the hospital were as follows: The urine was constantly negative with the exception of the presence of hemoglobin on the day following the transfusion. Blood showed a moderate anemia, but otherwise no noteworthy findings. The blood Wassermann was negative, blood sugar 49 mg. per cent; nonprotein nitrogen 32, and calcium 9.5 (after calcium administration). The icterus index was 11, van den Bergh direct 0, indirect immediate positive. The spinal fluid was as noted above and in addition revealed a sugar of 62 mg. per cent and a colloidal gold curve on one occasion of 0012444321. Hair and nail parings were negative for arsenic.

October 27 she was examined at home. She was doing quite well but still said no words. She walked normally, used her hands better but still had difficulty in apposing the fingers and thumb. The right knee jerk was exaggerated and there was unsustained right ankle clonus. She was given a tonic containing iron and vitamin B.

November 7 she was reexamined. Her progress had been satisfactory. She seemed to understand everything and tried very hard to talk. On examination she was quiet and cooperative, responded to all questions and directions, and said "yes" distinctly. She used her fingers and hands well. Neurologic examination was negative.

December 20 she was seen again. She was now saying everything and as far as the mother was concerned was perfectly normal.

She was again examined on March 27, 1937. She had developed a cough three weeks previously which turned out to be pertussis. Other than this the child had been doing well. Her speech, however, was very slow and careful in character; her facies was definitely mask-like, but there was no propulsive gait and no tremor.

COMMENT

The striking feature of this history is the administration of two toxic drugs to a small child with a presumable Vincent's stomatitis, sulpharsphenamine in two doses of 0.2 gm. and potassium chlorate in a total dose of 7-8 gm. During the course of this therapy the child developed evidences of a severe intoxication, the predominant symptoms of which soon pointed to involvement of the central nervous system. Which of these two drugs was responsible or whether the damage was due to their combined action is difficult to state. A careful review of the literature fails to reveal any report of central nervous system involvement as a part of potassium chlorate poisoning. Certain features of the acute symptomatology at the onset do fit in with such poisoning, however.

Gettler and St. George[1, 2] cite a case of fatal poisoning in a three-year-old boy in whom potassium chlorate solution had been prescribed as a gargle over the telephone. The mother misunderstood the directions and administered the solution by mouth with severe acute symptoms appearing after several doses followed by death in six hours. At autopsy the blood was chocolate brown and showed methemoglobin spectroscopically. The stomach was not corroded but was a slate gray color, all the organs were congested and grayish brown in color. The kidneys showed a parenchymatous nephrosis microscopically. Ansbacher[3] states that fatal potassium chlorate poisoning is rare at present. He reports a case in which the drug was taken by a young woman resulting in death. Bernstein[4] reported the case of an insane army officer who ate the entire contents of a tube of Pebeco tooth paste corresponding to about 7.5 gm. of potassium chlorate.

Cushny[5] states that the lethal dose of potassium chlorate varies greatly, as little as 1 gm. having proved fatal in a child while 40 to 50 gm. have been swallowed by adults without marked symptoms. McGuigan[6] also gives the minimal fatal dose as 1 gm. but states that in general 10 gm. or more are necessary to induce poisoning and 15 to 30 gm. are usually fatal. Gettler and St. George place the average fatal dose at 3 to 5 gm. According to Cushny, acute chlorate poisoning is first evidenced by severe and persistent vomiting with epigastric pain, diarrhea, and a dark cyanotic color of the skin and mucous membranes. Respirations are dyspneic, the pulse is rapid, feeble, and at times irregular, headache, giddiness, muscular weakness and restlessness supervene, and eventually in fatal cases coma and death follow. In the subacute cases vomiting and diarrhea are prominent, the vomitus frequently being bile stained, and sometimes bloody. The urine may be completely suppressed, or may be scanty and dark colored, later reddish brown containing hemoglobin, methemoglobin, and hematin in solution. The skin is often icteric and uremic symptoms may appear.

The action of potassium chlorate is on the red blood cells and especially on the hemoglobin with the formation of methemoglobin and hematin; laking occurring with the freeing of methemoglobin into the plasma. This action is due to the oxidizing property of chlorates. As a result asphyxia occurs and is the chief cause of the symptoms. In subacute cases products of red cell destruction obstruct the tubules of the kidney and in these cases fatality may be due to renal changes. Some of the products of hemoglobin destruction are deposited in the liver and spleen and bile pigments are increased in amount resulting in jaundice. Cushny states that chlorates have little or no direct effect upon the central nervous system or circulation though these are secondarily influenced by the asphyxia and renal changes. McGuigan says that fatality in acute cases may be attributed in part to potassium action on the heart and that fragmentation of heart muscle is a frequent cause of death.

The sudden onset of severe vomiting and marked muscular weakness in a child who had been receiving approximately 16 grains of potassium chlorate daily by mouth for a week or more is certainly significant. On one occasion the urine contained hemoglobin but inasmuch as this followed a blood transfusion it is difficult to consider it confirmatory evidence. An immediate positive indirect van den Bergh was also obtained. When this is combined with a complete lack of other findings to explain the severe symptomatology one is forced to attribute more than mere coincidence to the use of the potassium chlorate. The central nervous system involvement appeared to be definitely of a toxic rather than inflammatory nature. While it is impossible to incriminate either of the drugs positively one is inclined to suspect a possible causal relationship between one or both and the cerebral injury.

The reason for this report is to direct the attention of the medical practitioner to a major disaster which followed the internal administration of potassium chlorate in the treatment of a stomatitis. Lust[7] in discussing the use of potassium chlorate in Vincent's angina calls attention to its toxic properties with the statement "because of its marked hematoxic properties it is best to eliminate this drug entirely from pediatric practice and substitute for it harmless preparations. . ." Cushny similarly comments that it was introduced into therapeutics on the erroneous theory that it would supply oxygen to the tissues, that it hardly retards the growth of bacteria and no adequate explanation for its use in mouth and throat infections can be offered. In contrast to these statements, is that in Stevens' *Therapeutics:*[8] "In ulcerous stomatitis this salt is almost specific and may be used internally as well as locally. The dose for a child of three years is from 1 to 2 grains well diluted, every three hours. Benefit from its internal administration is to be attributed to its continuous elimination in the saliva." He does caution against its use in diphtheria and scarlet fever because of renal irritation. Such a statement appears to me to be most unfortunate. The physician who prescribed this medication said he had looked the subject up in *Holt's Diseases of Children* where he found a recommendation similar to the above. If so it must have been an old edition since the most recent revision by Holt and McIntosh[9] makes no mention of the internal administration of the drug and definitely states that locally the use of sodium perborate is preferable. I feel a revision of discussions on the therapy of stomatitis is in order with a definite warning against the internal administration of potassium chlorate and a caution as to its local use as well as the statement that systemic administration of arsenicals is hardly necessary in the average case. This child fortunately did not succumb but whether or not she will escape without residual changes still remains to be seen.

SUMMARY AND CONCLUSIONS

1. A severe toxic encephalopathy followed symptoms of acute poisoning in a child who received potassium chlorate by mouth and two injections of sulpharsphenamine in the treatment of a stomatitis.

2. While the literature contains reports of cases of accidental poisoning with potassium chlorate, an incident such as this with a resultant encephalopathy could not be found.

3. The causal relationship of the encephalopathy to the drugs used is not proved but is at least highly suggestive.

4. Potassium chlorate should never be administered internally in a child and its local use should be approached with caution. In fact there is justification for its complete removal from the pediatric armamentarium since other more efficient and innocuous oxidizing agents are available.

5. The necessity for prompt and bold action on the part of physicians is recognized. There are situations, however, where expectancy is eminently more desirable than action which carries harmful potentialities. The adage "primum nihil nocere" should still be carried uppermost in the physician's consciousness.

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CHOLECYSTITIS IN CHILDHOOD

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WHILE it is generally stated that cholecystitis is rare in children there have been over 300 such cases reported. Potter[1] in 1928 collected 226 cases, Holbrook[2] in 1934 added 27 more, Powers and Scheidell[3] in 1935, 14 additional, and Zelditch and his collaborators[4] in 1936 reported 32 cases. In addition there are numerous individual reports. It is the opinion of those who have discussed this subject that affections of the biliary passages in children are quite frequently responsible for recurrent abdominal pain.

The purposes of this presentation are to review briefly the cases of cholecystitis in children which have been observed at the Children's Hospital of Cincinnati and in the pediatric service of the Cincinnati General Hospital during the past twelve years, and to emphasize the essential features of the condition.

The present series comprises 8 cases (Table I). This is not an impressive number to have been admitted to two large institutions over a period of twelve years. It is probable that a much larger group, milder in degree, had been seen, often without recognition, in the outpatient department. Several additional cases observed are not included because of inadequate confirmatory evidence.

In the cases reported the primary complaint was abdominal pain. This varied in intensity and was usually located in the hypochondrium, particularly on the right side. Many of the reports in the literature stress the fact that the pain was in the region of the umbilicus and was referred to the right subcostal angle. In cases reported by Snyder,[5] Farr[6] and others, there were associated mild inflammatory changes in the appendix, and in these the pain was more indefinite in its localization and frequently more manifest in the right lower quadrant. The character of the pain may vary from a dull ache to intense cramp-like sensations. Nausea and frequently vomiting are accompanying symptoms, and there may be fever in varying degree.

Physical examination of these patients demonstrates tenderness and rigidity, more marked on the right side and usually in the upper quadrant. Varying degrees of jaundice may be present but it is more commonly absent. In some cases a tender mass may be palpated over the region of the gallbladder. In others the liver may be slightly enlarged. A moderate polymorphonuclear leucocytosis is usually associated.

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TABLE I

CASE PRESENTATION

SEX AND RACE	AGE IN YEARS	HISTORY	EXAMINATION	BILE DRAINAGE	HOW DIAGNOSED	RESULT
Female Colored	12	Recurrent attacks of upper abdominal pain, nausea, vomiting, chills and fever. Recent attack of typhoid fever.	Marked abdominal tenderness and rigidity, mostly in RUQ.* Palpable mass in RUQ. Temperature 102° F. WBC† 10,500. Polys 84%.	Six. Bile turbid with mucus, floccules and leucocytes. Culture —Typhoid.	Symptoms. Biliary returns.	Recovered following repeated bile drainages.
Female White	13	Recurrent attacks of upper abdominal pain, nausea, vomiting, and slight fever.	Marked abdominal tenderness and slight rigidity in RUQ. Tonsils inflamed. Temperature 99° F. WBC 13,500. Polys 70%. Oral cholecystography — gallbladder not visualized.	None.	Symptoms. Cholecystography. Operation: Gallbladder distended. Appendix normal.	Recovered following conservative treatment and appendectomy.
Male White	11	Sudden attack of upper abdominal pain, nausea, vomiting, and fever. Draining ear for three years. Attacks recurred in hospital, exaggerated by food, and localizing in RUQ.	Marked tenderness in RUQ with some rigidity. Bilateral otitis media. Temperature 101° F. WBC 28,000. Polys 88%. Oral cholecystography—gallbladder visualized normally.	None.	Symptoms. Operation: Gallbladder thick, distended, and adherent to the pancreas which was swollen and indurated. Spleen enlarged.	Recovered following cholecystectomy.
Female Colored	11	Recurrent attacks of upper abdominal pain, nausea, vomiting and fever.	Marked generalized abdominal tenderness and rigidity in the right lower quadrant. Temperature 101° F. WBC 12,400.	None.	Operation: Gallbladder thick, distended, and filled with stones. Acute hemorrhagic pancreatitis with bloody fluid in peritoneal cavity. Appendix normal.	Recovered following cholecystectomy.

Female White	15	Recurrent attacks of upper abdominal pain, nausea and slight fever usually occurring two to three hours after meals. Marked constipation.	Moderate abdominal tenderness and rigidity in RUQ. Questionable mass in RUQ. Liver slightly enlarged. Upper respiratory infection. Temperature 101° F.; WBC 16,000; Polys 72%. Oral cholecystography — gallbladder not visualized.	None.	Cholecystography. Operation: Gallbladder markedly distended. Appendix chronically diseased.	Recovered following appendectomy.
Female White	11	Severe attack of upper abdominal pain, nausea, and vomiting. Marked constipation. Slight fever. Questionable jaundice.	Marked abdominal tenderness and slight rigidity in RUQ. Slight jaundice. Temperature 100° F.; WBC 8,500; Polys 62%.	None.	Operation: Gallbladder markedly distended. Appendix chronically diseased and subhepatic in location.	Recovered following appendectomy.
Male Armenian	9	Recurrent attacks of abdominal pain, nausea, vomiting, chills and fever usually occurring after meals. Marked constipation. Questionable jaundice.	Extreme abdominal tenderness and rigidity. More marked in RUQ. Questionable jaundice. Dental caries. Sinus infection. Temperature 102° F.; WBC 13,500; Polys 84%; Icteric index 15; Stool examination. Lamblia Intestinalis. Oral cholecystography —gallbladder not visualized on two occasions during attacks; normal visualization between attacks following bile drainage.	Fifteen. Bile turbid with mucus, floccules and leucocytes. Numerous motile Lamblia Intestinalis. Culture negative.	Symptoms. Cholecystography. Bile drainages. Operation: Chronic adhesive perisplenitis, peritonitis, and hepatitis. Adhesions at base of gallbladder. Appendix normal. Liver enlarged. Spleen 3 times normal size. No Lamblia found in gallbladder contents. Culture—no growth.	Apparent clinical recovery following cholecystectomy. Symptoms were temporarily relieved by bile drainage.
Male White	6	Onset of right upper abdominal pain and tenderness during course of severe lobar pneumonia and empyemia thoracicus. Numerous tarry stools.	Abdomen markedly distended. Marked tenderness and rigidity in RUQ. Globular mass in RUQ. Liver enlarged. Temperature 102° F.	None.	Symptoms. Operation: Gallbladder thick, distended, and necrotic in several areas. It was adherent to the duodenum.	Recovery following thoracotomy and cholecystectomy.

*RUQ—right upper quadrant of abdomen.
†WBC—white blood cell count.

In five of our patients there was an associated infection of the respiratory passages. Focal infection is thought by most authors to be the exciting cause of cholecystitis, both in children and in adults. Beals,[7] who reviewed 64 cases in children, supports this theory and believes that it especially applies to children. Snyder[5] and Farr[6] believe that many cases develop as a metastatic complication of a chronically or subacutely inflamed appendix. In two of our own cases a chronically diseased appendix (pathologic report) was found at operation. Rosenow[8] states that in his opinion cholecystitis probably occurs when streptococci having an affinity for the gallbladder enter the blood stream. Cholecystitis has frequently been reported as a complication of scarlet fever.[2, 9, 10] Here, undoubtedly, streptococci are the exciting cause. Typhoid bacilli may give rise to an infection of the gallbladder, as in the case of the first patient presented. The first report of a series of such cases in children was that by Reid and Montgomery,[11] who recorded 18 cases observed at the Johns Hopkins Hospital prior to 1920, all of which were confirmed at operation. Mohr[12] reported one case directly following an attack of paratyphoid fever.

The finding of Lamblia intestinalis in the stool and in the biliary returns of one of our patients is of more than passing interest. Smithies,[13] in 1928, reviewed the literature concerning the pathogenicity of Lamblia intestinalis and stated that it has been recognized that under certain circumstances they are decidedly pathogenic. In the lower bowel they may give rise to ulcerative colitis and ileitis. When found in the duodenum they may be pathogenic and, in addition, when found here, they may also be harbored in the gallbladder. Smithies' deductions are based on 5,000 biliary drainages and the finding of Lamblia in massive numbers in the gallbladder when the patients who exhibited the parasites in the biliary returns were subjected to operation. The chronic splenitis and multiple adhesions around the gallbladder, liver, and small intestine in our patient are similar to the conditions found at operation in one of his patients. Golob[14] states Lamblia infestation of the gallbladder may simulate acute cholecystitis by obstructing the cystic duct. He reported two such cases. Westphal and Georgi,[15] Calder and Rigdon,[16] Guerstein and Reydermann,[17] and Zelditch and his collaborators[4] have all reported cases in which Lamblia were established as the causative agent. The last mentioned authors reported 32 cases of cholecystitis in children, 12 of these having Lamblia in the biliary returns. Lichta[18] and Kouznetzoff[19] also believe Lamblia are etiologic factors in certain cases of cholecystitis. It should be noted, however, that some authors as Paulson and Andrews[20] and Boeck[21] believe Lamblia to be nonpathogenic.

The technique of biliary drainage is well known[22] and consists in the introduction of a jutte tube into the duodenum and the injection of a few cubic centimeters of a 25 per cent magnesium sulfate solution

through the tube to promote the flow of bile. The finding of mucus, floccules, leucocytes, parasites, or crystals of cholesterol in the "B" or bladder bile is considered evidence of gallbladder disease. The procedure has been found practical in children and even in infants. In one of our patients it was applied with satisfactory results in diagnosis and treatment, and in another, the diagnosis was made in this manner although operation was later performed. Smithies,[13] who employed the method extensively, feels that it is a valuable aid in diagnosis and treatment of gallbladder disease in children. Guerstein and Reydermann[17] have also found it helpful. Zelditch and his collaborators[4] have been doing biliary drainages routinely in the out-patient department at Kiew since 1931. They thus have a large series of control cases on which to base their findings in 12 cases of Lamblia infestation. Every patient exhibited abnormal findings in the biliary returns which disappeared after repeated drainages. Coincident with the return of the bile to normal the symptoms were ameliorated.

Oral cholecystography is widely used in the diagnosis of gallbladder disturbances in adults. It is equally applicable in children as demonstrated by Reviglio[23] in 1929. Hamilton, Rich and Bisgard[24] also recommend oral cholecystography in children. In three patients of the present series the diagnosis was made by roentgenogram. In one of these, visualization of the gallbladder did not occur on the two occasions before biliary drainage was begun, but following this the gallbladder filled and emptied normally. In a fourth patient a normal roentgenogram was obtained but the gallbladder was found to be definitely diseased at operation. It has already been stated that Zelditch and his collaborators obtained abnormal roentgenographic findings in all of their patients. Holbrook[2] reported one patient in whose case the gallbladder failed to visualize on two occasions, and a diseased organ was found at operation. Beals' patient[7] was diagnosed cholelithiasis by roentgenographic study, and this was also confirmed at operation. Evarts Graham,[25] in discussing Beals' paper, stated that at the Children's Hospital in St. Louis about 12 unreported cases of cholecystitis have been seen, in several of which the diagnosis was made by cholecystography. Some of these were confirmed at operation. The others were classified as chronic and not operated upon.

The majority of cases of cholecystitis reported in children have been diagnosed acute appendicitis and it has not been until operation or necropsy that the actual condition has been determined. This is unfortunate, especially in view of the bearing accurate diagnosis has on the subsequent treatment. In Potter's 226 collected cases,[1] 140 had stones, 48 did not, and in 38 there was no statement as to their presence or absence. Since Potter's paper, in over 70 per cent of the cases reported there was cholecystitis without stones. It is the generally accepted practice among experienced surgeons to delay operation in these

patients until the symptoms have subsided and it is, therefore, extremely important to establish the diagnosis, since the treatment of the conditions which might be confused with cholecystitis is quite different.

Among the conditions to be considered in the differential diagnosis are appendicitis, pyelonephritis, perinephric abscess, nephrolithiasis, subdiaphragmatic abscess, diaphragmatic pleurisy, catarrhal jaundice, pneumonia, pericarditis, pancreatitis, peptic ulcer, and duodenitis. The association of acute pancreatitis and cholelithiasis, as in the cases of the third and fourth patients presented, is not infrequent in adults.

SUMMARY AND CONCLUSIONS

1. Eight cases of cholecystitis in children are reported.

2. Cholecystitis is not infrequently the cause of unexplained abdominal pain in children. Often these patients are seen in the outpatient clinic or in office practice and are not subjected to further study. The pain disappears with symptomatic treatment only to recur at variable intervals and the condition is classified as mild gastro-enteritis, indigestion, or subacute appendicitis.

3. That Lamblia intestinalis may be an etiologic factor in cholecystitis is mentioned.

4. There should be careful study of all children who manifest obscure abdominal pain. The possibility of cholecystitis as one of the causes is emphasized.

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THE DEVELOPMENTAL HISTORY OF STUTTERING CHILDREN

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THE PROBLEM, THE SOURCE OF MATERIAL, AND THE GENERAL PROCEDURE

EVERY speech clinician has entertained suspicions about the normal physical development of the stuttering child. The clinician realizes that parents seeking an explanation for the disorder very naturally exaggerate the child's deviations from the norm. He is inclined, however, in view of the increasing emphasis on hereditary and biologic factors in stuttering, to listen with some credence to the history of an atypical development. Are the first five years of the stutterer's life entirely normal? Will his developmental record of delivery, birth weight, feeding, walking, and talking compare favorably with that of a child with fluent speech? Does he vary only in one single respect from the nonstutterer?

These questions delineate the problem of the study. Previously, surveys have been made on such developmental criteria as handedness, emotional growth, and social adjustment. We should like to approach the problem by investigating the medical records of these children entered in clinics in early infancy. Through the cooperation of Bobs Roberts, Children's Memorial, and Michael Reese Hospitals, and the Rush Medical Clinic in Chicago we were able to assemble medical histories on 500 stuttering children. The assistance of the Jewish Home Finding Society, the Illinois Institute for Juvenile Research, the Elizabeth McCormick Fund, and the Chicago Orphans Asylum made possible the collection of 500 medical records of nonstuttering children entered routinely for pediatric care.

We were faced at the outset with a very real difficulty: there was a comparatively small number of records which embraced information on all the items in which we were interested. The groups, therefore, vary in size and in certain instances the number is too small to warrant generalization. A most important subject to us, the development of the child's laterality, is not a part of the routine case history outline. The records of the stutterers occasionally embraced information on this point, but the records of the control group rarely mentioned this factor unless the case involved a nervous disorder. No comparison, therefore, can be made on this point.

FINDINGS

1. *Prenatal Conditions and Delivery.* Only distinctly abnormal or pathologic conditions were noted in the record concerning the fetal life of the stutterer. No index of the general condition of the mother during

pregnancy could be secured. An examination of the data on illnesses experienced by the mothers of the two groups, stuttering and control, did not show any material differences except in one particular. In four cases, mothers of stutterers were afflicted with exophthalmic goiter and thyrotoxicosis during pregnancy; there is no mention of this disorder in the records of the control group. The writer recalls that in reading 200 case records of exophthalmic goiter (reported elsewhere), two made mention of the fact that a stutter present in childhood had recurred with the exacerbation of the thyroid condition. In another case history, a case of cretinism treated from infancy, an increase in the dosage of thyroxin suddenly brought on stuttering. Whether the connection between an endocrine dysfunction and stuttering is coincidental or real cannot be determined with the number of cases at hand.

The type of delivery was commented upon by the two groups in practically equal numbers. Reports for 227 stutterers and 232 nonstutterers were available. Table I presents the salient data.

TABLE I

TYPE OF DELIVERY

	STUTTERERS (227)	CONTROL (232)
Normal	205	215
Instrument	21	19
Prolonged labor	13	8
Premature	12	13
Breech presentation	6	1
Cyanosis	6	2
Injury to infant	3	2
Brain hemorrhage (infant)	2	1
Caesarian	1	4

The figures show no significant differences between the two groups in type of delivery.

2. *Birth Weight.* The birth weight of the two groups may be compared although it must be recognized that a greater number was reported for the control group than for the stutterers (Table II).

TABLE II

BIRTH WEIGHT

	STUTTERERS (71)	CONTROL (145)
Mean (in lb.)	7.461	7.131
Mode (in lb.)	7.500	8.000
Median (in lb.)	7.610	7.340
Standard deviation	7.331	6.794
Critical ratio (*Diff.* / S. D. diff.)		0.319

The critical ratio is low, 0.319, indicating that there are only 59 chances in 100 that the true difference between the groups is greater than zero. Compared with Hardy and Hoefer's study[1] of 406 normal

children, both stuttering and control groups fall below their mean of 8.54, but when compared with Faber's study[2] of 644 normal infants, the mean birth weight of 7.5 pounds which he establishes is matched exactly by the stutterers. The control group again falls below the norm.

3. *Feeding.* The two groups reported in approximately equal numbers on the type of feeding (Table III).

TABLE III

FEEDING: TYPE AND PERIOD

A. TYPE OF FEEDING	STUTTERERS (189)	CONTROL (201)
Breast	126	126
Artificial	52	51
Breast-Artificial	13	24
B. PERIOD OF BREAST FEEDING (IN MONTHS)	**STUTTERERS (71)**	**CONTROL (89)**
Mean	10.634	8.172
Median	10.625	9.330
Mode	12.000	12.000
Standard deviation	5.600	4.445
Critical ratio		3.255

A comparison of the means reveals that the period of breast feeding for the stutterers was 2.5 months longer than for the control group. The critical ratio, 3.255, indicates that there are 100 chances in 100 that there is a true difference greater than zero between the two groups. So many variables, however, enter into the length of the nursing period that it is not possible to give a satisfactory interpretation of the difference. Seasonal considerations, i.e., the prevalent theory that it is unwise to wean children during the summer, economic status, traditional practices of the social group to which the mother belongs, and nationality of the parents are factors which, if fully known, might minimize the differences between the two groups.

4. *Walking.* Although the largest number in both the stutterers' and control groups began to walk at twelve months, the range among the stutterers is considerably wider (two times). The mean and the median show an appreciable difference between the two groups (Table IV).

TABLE IV

WALKING (AGE IN MONTHS)

STUTTERERS (210)					CONTROL (226)					
No.	mode	median	mean	S. D.	No.	mode	median	mean	S. D.	C. R.*
210	12	13.61	14.8	4.79	226	12	12.83	13.54	3.43	1.59

*Critical ratio: $\frac{\text{Difference}}{\text{S. D. diff.}}$

If we leave out of consideration the cases of extreme retardation in walking in the stuttering group, because in three of the five cases pathologic conditions interfering with the acquisition of normal control are

noted in the record, we still find that an appreciably larger number of stutterers is retarded in learning to walk. The incidence of rickets is greater in the control group than in the stutterers' group, and therefore, it cannot be considered a factor militating against the development of walking in the stutterers.

In the study by Hardy and Hoefer[3] the mean for the total group of 403 children was 13.01 with a standard deviation of 2.93. It will be noted that the nonstutterers in our group are accelerated slightly beyond the mean established by Hardy and Hoefer but that the stuttering group falls definitely below the norm. The average for the control group is slightly higher than the mean established by Terman[4] for 1,000 gifted children (12.98). In comparison with Terman's figures the stutterers are retarded by 1.82 months, the control group by 0.56 months. The critical ratio expressing the difference between the two groups in this study is 1.59, indicating that there are approximately 86 chances in 100 that the true difference is greater than zero.

There is some indication that the stutterers are atypical in the acquisition of motor skills other than speech.

5. *Speech.* Because the onset of speech is regarded as an excellent sign of normal neural growth, it seems strange that no study previously has been made on the age at which speech begins in the stutterer. We can find no record of such an investigation. Several scholars, however, have given attention to the articulatory and vocal problems of stutterers during nonstuttering speech.

Dr. Elizabeth McDowell,[5] in testing 60 stutterers and a similar number in a control group for speech difficulties other than stuttering, fails "to find a marked disparity between the groups." Mrs. McDowell questions, however, the value of her data because of "certain varying factors in the testing situation brought on by the subjective nature of the scoring."

Dr. Robert West[6] reports that "there are certain demonstrable differences between stutterers and nonstutterers aside from the spasms that occur during speech of the former. The chief of these are: (1) The slowness of diadochokinesis of the articulatory muscles of the stutterer. (2) The lack of inflection of the vocal tone. It may be that the two are related, and that both are caused by muscular spasticity. In slowness of diadochokinesis the stutterers are much like the spastic. The lack of inflection of the stutterers can be noted by the trained ear. After a considerable experience with stutterers, the listener will become aware of the tenseness and inflexibility of the stutterer's vowel sounds. The stutterer's voice shows changes of pitch from word to word, and even from syllable to syllable, but during the utterance of a unit-voiced sound the pitch is inflexible. The normal speaker practically never holds

a vowel level in pitch. . . His condition in this regard may be thought of as being half way between normal speech and paralytic speech, or as wavering between these two states."

In this study we have collected data on two processes in speech development: (1) the beginning of speech or "first words"; (2) the development of a speech which may be understood by members outside

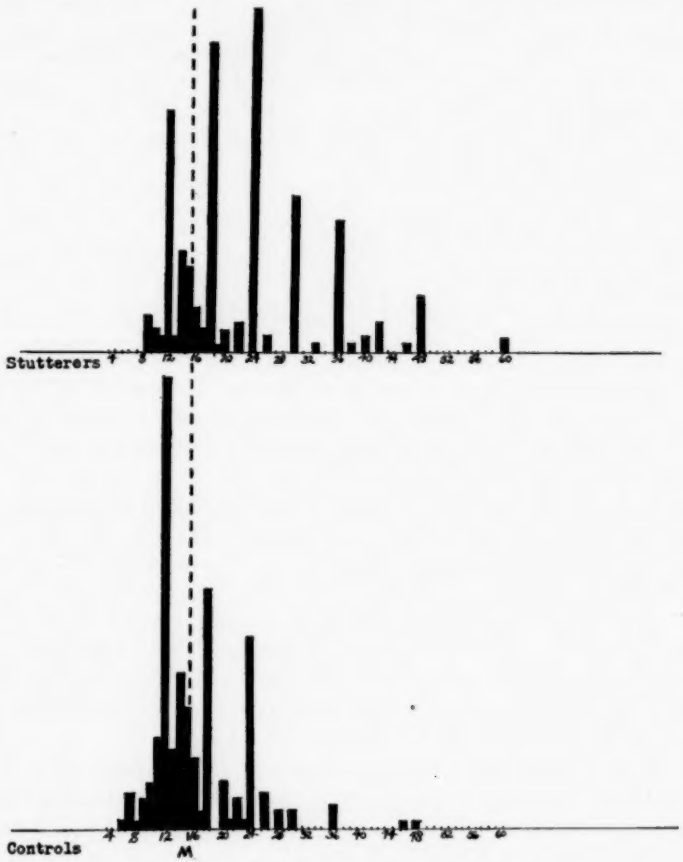

Fig. 1.—Age of onset of speech (in months).

of the immediate family, and hereafter designated as "intelligible speech." Although the figures from other studies are presented, it does not seem wise to rely to any extent upon these figures for valid comparisons because projects not specifically concerned with speech development do not differentiate between the utterance of single words and the development of intelligible, connected speech. The two processes may not be closely linked in time. The work by D. A. McCarthy[7] is

an exception because he is concerned with the language development of the preschool child. McCarthy concludes that "the absence of comprehensible speech in a child of two and one-half years of age should be considered a definitely abnormal condition." Comparative Tables V and VI and Figs. 1 and 2 present the salient data.

TABLE V

FIRST WORDS (AGE IN MONTHS)

	NO.	MEDIAN	MODE	MEAN	S. D.	CRITICAL RATIO
Stutterers	243	18.45	24	23.54	10.21	8.49
Control	252	14.25	12	16.12	6.09	
Hardy-Hoefer[8]	364			14.19	5.39	
Mead[9]	50			15.32	3.0	

TABLE VI

INTELLIGIBLE SPEECH (AGE IN MONTHS)

	NO.	MEDIAN	MODE	MEAN	S. D.	CRITICAL RATIO
Stutterers	140	30.48	30	36.21	14.2	6.854
Control	154	22.38	20	24.18	7.9	

The findings reveal that the stutterer is definitely retarded in the initiation and development of intelligible speech. The very large critical ratio, 6.854, denotes a reliable difference between the two groups. The ratio indicates that there are 100 chances in 100 that the true difference is greater than zero.

In 39 clinic reports the figures revealing retardation in speech were reinforced by a specific statement that the child was definitely retarded in learning to talk; 38 clinic records noted the presence of infantile perseveration; in 40 cases physicians recorded very indistinct speech; on 17 charts lisping was noted. In many instances the first visit to the clinic was made because the mother was concerned over the child's inability to talk. When speech finally was initiated, it was accompanied by stuttering. This is the typical clinical report corroborated by physician, psychologist, and social worker.

It might be argued that these children represent a group with a low intellectual rating. The average intelligence quotient for 166 stutterers on whom reports were available was 0.992. In the control group there were 161 records containing this information. The mean for this group was 0.976. Both classes are within the range of high normal intelligence and yet there is an appreciable difference between them in onset of speech. The difference cannot be accounted for on the basis of low intelligence. The stutterer evidently begins life with a specific deficiency in the armamentarium necessary for speech.

Discussion of the findings.—On the basis of these records the stutterers differ most significantly from the control group in one respect, the initiation and development of intelligible speech. So many factors

enter into the complex picture of stuttering that only a few suggestions may be safely offered to explain the stutterer's retardation. The most valid inference is that the stutterer begins life with a defective armamentarium for speech. This neural arrest some workers now believe to be inherited. Others hold that a prenatal or postnatal toxic invasion of the nervous system has damaged the speech centers and routes. In some cases only infantile perseveration or lisping bears evidence of the damage. In other cases the synergy is so seriously impaired that stut-

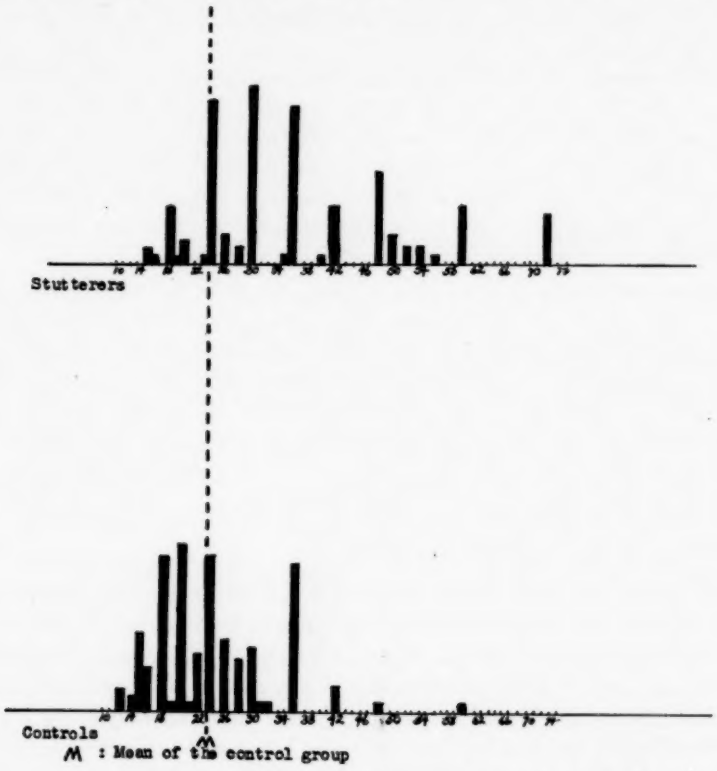

Fig. 2.—Age of development of intelligible speech (in months).

tering results. So the argument runs. The inference of a natively defective armamentarium receives indirect support from Flechsig's[10] study of the embryology of the brain. It should be remembered that the White House Conference survey established the fact that "the ratios of stuttering boys to girls above thirty-six months of age vary all the way from 3 over 1 to 8 over 1."[11] Stuttering and maleness evidently are linked. It is interesting, therefore, to note that Karlin and Kennedy,[12] interpreting Flechsig's findings, suggest that the later development of

speech in the male may be caused by a later myelinization of the nerve tracts in the speech pattern. Whether the defect is one of temporary or permanent ablation, or impairment of certain neural centers or pathways, or of a delay in myelinization of the fibers in the speech pattern is not known. In this connection it should be noted that twinning is more frequent in stuttering families[13] and that twins are retarded in their language development.[14]

Those who believe that stuttering is a functional disorder caused by an emotional maladjustment may find this hypothesis, at first glance, a direct contradiction to their views. It should be remembered, however, that emotional disturbances may be the secondary or precipitating cause, not the primary cause of the stuttering. There may be a good many potential stutterers who never break over into stuttering. Their "margins of safety" are wide. If the environment, however, is unsatisfactory, then the child may realize his potentialities for stuttering. The provoking cause, indeed, is the emotional problem but the basic cause may be a natively inferior mechanism for speech.

The same warrant of consistency may be given to those who hold that stuttering is set off by some illness accompanied by a high fever. Endowed by inheritance with an inferior speech mechanism, the potential stutterer may "ride the waves" successfully until a temporary infection or nervous disorder engulfs him. The illness may be of short duration, but the damage may be sufficient to precipitate stuttering.

All in all, whatever theory one accepts, he is forced to recognize the strong possibility of a genic complex in stuttering.

CONCLUSIONS

1. There was no demonstrable difference between the two groups in the conditions associated with the pregnancy of the mother and delivery.

2. The mean birth weight of the stuttering group matched exactly the mean birth weight established by Faber. The critical ratio between the stuttering group and the control group indicated that there were 59 chances in 100 that the real difference between the groups is greater than zero.

3. The average length of breast feeding was greater among the stutterers than among the control group. Although the critical ratio points strongly to a true difference, a large number of variables precludes a positive finding.

4. The stuttering children were retarded in learning to walk when compared with a similar group of nonstuttering children. The critical ratio indicates that there are 86 chances in 100 that the true difference is greater than zero.

5. The stuttering children showed a serious retardation both in the initiation of speech and in the development of intelligible speech. The very large critical ratios indicate that there are 100 chances in 100 that the true differences are greater than zero.

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THE EMOTIONAL AND SOCIAL DEVELOPMENT OF GIRLS WITH HEART DISEASE

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FOR the past fifteen years we have had the opportunity to study a large group of girls with rheumatic heart disease. These children were under the observation of one group of observers throughout a greater part of their latter childhood and practically their entire adolescent period. Although the control varied slightly in the two different periods of observation, the personnel that studied the groups was practically identical throughout the entire fifteen years. In addition to the physical problems arising on account of their cardiac disease, the emotional and social development of these children offered an interesting field for study.

Past studies of children with rheumatic heart disease have emphasized primarily the pathology and the prognosis. Although in some institutions attempts were made to establish a satisfactory social adjustment, particularly along vocational lines, none of these was very intensive nor have they been very fully studied.

As our experience with the children who had spent a residential period at the cardiac school increased, we were tremendously impressed by the absence of any instances of real emotional or social difficulties based on the cardiac disease. An estimate of this kind based purely on clinical impressions without substantiation either from specific studies or statistical data, was open to very much doubt. Ordinarily, these children passing from hospital to hospital, out-patient clinic to out-patient clinic diverse in approaches and management techniques, do not offer the necessary continuity for a study in development. It is only under conditions such as we have been able to establish that a continuous record may be kept which offers material of comparative value in these studies.

MATERIAL

In order to study the effects of chronic disease and its necessary limitations on the development of children with cardiac disease, a group of 21 girls, who at the present time range between twelve and eighteen years was selected for study. This group was selected from about 130 girls with rheumatic disease, associated with established and persistent cardiac involvement. The method of selection was simply to utilize children

From the Theresa Grotto Residential School for Cardiac Children.
Master's Dissertation, Fordham University, 1937.

of the older age group that were available. In the period from 1923 to 1928 the group was under our control at the Beth Israel Hospital in the Ambulatory Cardiac Clinic, and from the beginning of 1929 up to the present time, the group has been treated at the Theresa Grotto Residential School for Cardiac Children at Caldwell, N. J. All the children studied have had residential time at the cardiac home. The clinic group consisted of 60 children, 21 of whom are known to be dead, 19 whose records have been lost, and 20 who have been included in the present group for study. Seventy other children have been added since 1929. The mortality of the group that has had a residential period at Theresa Grotto has been 6 out of the 90 children under observation for periods ranging from one to seven years.

The institution is situated in the country about 15 miles from Newark, has adequate grounds, and a building housing 12 children. There is a resident nurse, a resident teacher, and the necessary facilities for the medical study of the group.

In the organization of the personnel, there is only one outstanding difference from the usual plan in institutions for the care of the cardiac child. This group is in the direct charge of a pediatrician with the cardiologist, social workers, psychiatrists, and others acting as consultants. One of the primary results of this arrangement of personnel is that an attempt is made to evaluate and handle not only the physical disability but the mental problems that arise.

The Theresa Grotto is primarily an experimental clinic for the development of procedures and methodology to handle cardiac children to the best advantage. Practically all of the children accepted for study have come from the lower social and economic group. With the great number of children afflicted with rheumatic heart disease, and the small capacity of the institution, a selection was made of those we felt most required the care and help of an organized group.

According to the best available statistics, the incidence of rheumatic heart disease in the schools of our community is approximately 1 per cent. Due to the limited facilities available, we have not as yet been able to develop a service for both sexes, and only girls have been studied.

Rheumatic heart disease, as it manifests itself in childhood and early adolescence is a long drawn-out chronic infection with intermittent periods of exacerbation and remission. The children are admitted to the institution after an attack of cardiac decompensation for which they have been hospitalized, or when found with active signs of rheumatism or rheumatic heart disease.

As will be seen in Table I, the age of the discovery of heart disease varies from two to ten years in the group studied with an average age of seven and one-half years. This is not the age at which the heart disease is acquired, but the age at which, for the first time, the family

had definite knowledge that the child's heart was affected. Table I also shows the number of hospital admissions for decompensation. This is a rather accurate criterion as to the severity of the involvement. It will be noted that the greatest number of decompensations are in cases 6 and 18, one child having 3 and the other 4. These 2 girls are the only ones in our list that have involvement of both the aortic and the mitral valves.

TABLE I

CASE NO.	PRESENT AGE	AGE AT DISCOVERY OF HEART DISEASE	NUMBER OF HOSPITALIZATIONS OR THE DECOMPENSATION	TYPE OF VALVULAR LESION
1	12	7	1	Mitral
2	13	5	1	Mitral
3	13	8	1	Mitral
4	13	8	0	Mitral
5	13	10	0	Mitral
6	13	10	3	Mitral and aortic
7	14	5	0	Mitral
8	14	2	1	Mitral
9	14	6	1	Mitral
10	15	6	1	Mitral
11	15	10	1	Mitral
12	16	7	2	Mitral
13	16	6	0	Mitral
14	16	7	0	Mitral
15	16	5	2	Mitral
16	17	9	0	Mitral
17	17	7	0	Mitral
18	17	9	4	Mitral and aortic
19	17	9	0	Mitral
20	17	6	3	Mitral
21	18	7	1	Mitral
Average		7.5	1.05	

The average length of stay in the institution was about twelve months and the average stay of the children of the group under consideration was fourteen months. As will be seen in Table II, the age of first admission to the Theresa Grotto Home varied from seven to thirteen years. Ordinarily, the child was admitted only once, but in a number of cases 2 or 3 admissions are noted. These readmissions followed acute exacerbations of the original infection while the child was at home, severe enough to demand hospitalization, and later, return to the residential school. The condition of the child on discharge as given in

Table II follows the classification of the American Heart Association. The weight gains also given in this table are an indication frequently not only of the physical improvement of the child, but of the disappearance of emotional factors that influenced the nutrition.

TABLE II

CASE NO.	AGE ON ADMISSION TO THERESA GROTTO	NUMBER OF ADMISSIONS	TOTAL STAY (MONTHS)	CONDITION ON DISCHARGE	WEIGHT GAINED (POUNDS)
1	10	1	10	11A*	10
2	7	2	14	1	13
3	9	1	13	1	6
4	11	1	11	11A	22
5	10	1	16	1	35
6	12	1	12	11A	13
7	7	1	13	1	8
8	10	1	17	11A	30
9	10	1	11	1	20
10	8	1	23	11A	11
11	11	1	14	1	16
12	11	1	12	1	27
13	9	1	13	1	10
14	9	2	11	11A	12
15	11	2	24	11A	21
16	11	2	10	11A	21
17	9	1	13	1	21
18	12	3	30	11B	35
19	13	1	3	1	10
20	11	3	14	11A	35
21	9	1	10	11A	12

*Classification: 1, No symptoms; 11A, symptoms on moderate exertion; 11B, symptoms on slight exertion.

Social service surveys have been made on all of the children by the social service units of the various referring hospitals. Psychiatric service and mental hygiene studies have been done by Dr. Fuller of the Graystone Park Unit, Department of Mental Hygiene, State of New Jersey. In addition to the studies by the mental hygiene unit, specific recommendations were made as to the management of the cases admitted. These procedures were carried out in the institution, and the mental hygiene unit further furnished considerable help in readjusting the home conditions of the children in preparation for their return after the stay at Theresa Grotto. No child whose intelligence was below the normal range was accepted into this group. Many of the children were admitted with definite psychic difficulties already established.

METHOD OF STUDY

The methods adopted for the study were practical only because of the fact that the children had been under the medical care of the writer for a long period of time. All the cases had been personally controlled by the author for periods of at least four years, and in some cases, as long as twelve years. This long time contact had established both with the child and the family the necessary rapport so that the information desired was readily obtainable and the difficulties ordinarily experienced in establishing confidential contacts were obviated. Records extending back over a period of many years, medical, social, economic and psychiatric, were available from the files.

In every case, at least one primary complete social service survey made at or before the time of the admission of the child to the residential school was available. There also was a complete psychologic and psychiatric survey made immediately after admission. These primary studies have been used to furnish the background for further development, giving a definite point of departure for the comparative studies carried out later. Separate interviews were arranged for the child and the parent. These interviews were planned on the basis of conferences for vocational guidance, and as far as the child knew, there was no record made during the interview.

In addition to the discussion of vocational guidance questions, a rather intensive analysis was attempted as to the general adjustment of the child, particularly in emotional and social fields. These interviews were recorded verbatim by a stenographer in the adjoining room. The summaries of the case histories submitted were made from this interview material. In most cases, only one interview was obtained.

In addition to a study of the material so obtained, two types of objective testing were utilized. "The Adjustment Inventory"[1] of Bell for the classification of the home, health, social, and emotional adjustment, and the "Personality Schedule"[2] of Thurstone were employed. Wherever necessary, further psychiatric studies were made.

The primary difficulty on admission has been the reaction of the child to an overprotective home environment. In our experience it has been impossible to treat these children in their own homes without this factor entering to a very great extent. Frequently this factor enters in the primary examination conducted on admission.

One child admitted to the institution, although fairly well compensated, had not walked within two years of the admission date. In another case, the child gave evidence of so much disturbance at the time of her admission, that the symptomatology might have been ascribed to cerebral damage. Her speech was interfered with, she was extremely distractive, and entirely antisocial. Under observation in the institution, where she had been admitted after the psychiatrist's evaluation of

her mentality as approximately normal, within a year the physical evidence of disorganization disappeared, and although her social and emotional adjustment is not everything that might be desired, it is at least within the accepted standards for normally mental children.

CASE HISTORIES

We will first present a résumé of the case histories as obtained from the interviews cited above. In addition to this interview material there has been incorporated into these summaries information concerning the child and the family obtained from other children and from the social workers who were in charge of these cases. All of these case summaries are divided into two parts. The first is a description of the status of the child on or about the time of its primary admission to this group. The second is the status, as closely as we have been able to determine, of the child at the present time. It will be noted that the interval of time between these summaries varies from two to eleven years.

SUMMARIES OF CASES

CASE 1.—*At ten years.* The patient is a small Jewish girl. The heart disease was first recognized at seven years and she was hospitalized for decompensation for ten months at that time, at Beth Israel Hospital. The social worker states, "Due to the intelligence of the parents, the child should straighten out." The psychiatrist reports, "No mental hygiene problem, very superior intelligence."

At twelve years. The father is a university graduate, admitted to the bar in New Jersey but has never practiced. He was a small manufacturer until the depression, after which the family, although not on official relief, was supported to a very great extent by relatives. The mother is of the aggressive type, extremely disappointed in her present status. The illness of the child has been a matter of grave concern to both parents, particularly because some recommendations that were made were financially impractical. The child is extremely bright, highly successful scholastically with an adult comprehension of the difficulties that exist. One of the major factors in the lack of friends and associates has been the feeling of social misplacement. Although only twelve years old, she has established a definite boy and girl friendship that is probably thoroughly dramatized along the lines of the romantic literature of the period which she reads. In these daydreams she apparently is finding adequate satisfaction for her lack of personal social contacts. Many of her reactions are old for her age, and her reserve in the interview was very noticeable. This was not a shyness based on inadequacy but rather the well-poised control of a well-developed child. This child's emotional difficulties are related to an unsatisfactory home and economic situation rather than to her physical condition. She has never utilized her physical handicap as a method of obtaining desired ends.

CASE 2.—*At seven years.* The first knowledge of heart disease in this child was at the age of five years. She was decompensated at six years and hospitalized four months. On admission, the psychiatrist reported, "High average intelligence, attention-getting mechanisms on a basis of the cardiac pathology." Social worker's report, "All children in the family present potential behavior problems due to the lack of discipline. All the children complain about favoritism to this child on account of her physical condition."

At thirteen years. This patient is an Italian girl, living in a mixed Italian and colored neighborhood. She is greatly restricted by the parents. The element of over-

protectiveness in this situation is counteracted by the fact that this attitude is a customary and accepted attitude in their own social group. This child is attractive and well developed for her age. She was thoroughly at home and well poised, and spoke readily without hesitation. There are no difficulties at the present time with the other children in the family and there is no attempt to utilize the cardiac pathology to obtain desired satisfaction. Socially, she is very well adjusted.

CASE 3.—*At nine years.* The child is definitely below average in physical development. Her intelligence is of low average grade and she presents no specific mental hygiene problem. There is very little attempt at attention-getting on the basis of her cardiac pathology.

At thirteen years. The case presents a thirteen-year-old Italian girl, well developed, of low average intelligence. She is one of 6 children in a first generation Italian family. The restrictions of this social group are evident but accepted. She has congenital syphilis and is receiving treatment. She is a rather self-contained child and resents anything that reminds her of her physical disability. She was unwilling to come to the interview, but after she arrived, cooperated fairly well. Her interests and accomplishments are within the range of her ability. Her social adjustment is fairly good. Apparently in some of her social relationships, i.e., her ability to escape from routine gymnasium work in schools, and the fact that some of her friends are somewhat careful as to her feelings concerning her heart condition, advantage is taken by the child of her cardiac condition. In spite of this acceptance and the utilization of her heart lesion, within very marked limitations, she seems to have no other reactions to her handicap.

CASE 4.—*At eleven years.* In this girl the first heart involvement was known at eight years. The social service worker reports, "Child is nervous and irritable, sleeps poorly, goes to bed rather late, is rather difficult to manage, cries easily, becomes sullen." Psychiatrist's estimation, "Average intelligence, easily distracted and not cooperative." Home conditions very poor, economic conditions very bad.

At thirteen years. The patient is an average Italian girl, well developed, with an extremely pleasant manner, a ready smile, a rapid answer. She is above her group both in intelligence and poise. She seems to have no difficulties of any kind in her social adjustment.

CASE 5.—*At ten years.* The child was admitted from an orphanage. She was a normally intelligent child with no special mental hygiene problems.

At thirteen years. The girl is well developed, about one year behind in scholastic work due to lack of schooling. She lacks the poise and assurance that many of the girls of this group have, and exhibits a certain amount of shyness. She is having a rather trying time; her mother died four years ago, her father has remarried, and the child says the stepmother is extremely jealous of the children. Her emotional problems, although very real and probably interfering to a certain extent with her social adjustment, are not on the basis of the heart disease but rather on the basis of the home situation.

CASE 6.—*At twelve years.* This twelve-year-old girl has been very sick, and in the last three years has spent most of her time in hospitals. There is no mental hygiene problem except that due to prolonged invalidism.

At thirteen years. The child is poorly developed. She is apparently somewhat shy in ordinary contacts, but probably more at home in the interview due to our longtime contact. She shows no evidence of any emotional blockage due to her heart condition except as she says that under certain conditions she has a rapid heart beat which she believes to be visible. When this occurs, she is shy, nervous, and attempts to withdraw from public appearances. However, this condition is not frequent, and in spite of it, she is secretary of her class, sings solo parts in the

glee club organization, and is chairman of the current events club in school. There are, however, factors in this child's home that may produce difficulties in the future.

CASE 7.—*At seven years.* The first knowledge of heart disease in this child was at five years. The psychiatrist reports, "Inferior intelligence, marked inferiority feelings, shy and retiring, probably on a basis of cardiac condition."

At fifteen years. The patient is a well-developed Polish girl of a low normal group intellectually, who is having many real difficulties in adjustment. Although perfectly at home in the interview, her general reactions are those of extreme shyness and inability to make friends. Her inferiority feelings have been exaggerated by her low school placement which to a very great extent, has not been due to her illness but to her lack of intellectual capacity. She explains her inability to make friends as based on a lack of desire to mix with Italian children socially. This probably is also a reaction to her own feeling of inferiority. Although this child presents many problems, there is no reason from the interview to believe that any of these problems has been aggravated by her physical condition, but rather to believe that the group training to which she has been subjected at the institution may have helped her to make some classroom adjustments that otherwise could not have been possible.

CASE 8.—*At ten years.* The first knowledge of heart disease was at two years. She was admitted to Baby's Hospital at this time with pneumonia and empyema. She had recurrent attacks of carditis in January or February in each year for the next four or five years. At no time has there been any decompensation. This child on admission presented evidence of psychic disturbance on the basis of an overprotective home environment.

At fifteen years. Economic conditions in this home were unbelievably bad. The father was killed two and one-half years previously, and there has been extreme poverty since that time. The child is very sensitive to home conditions, to her lack of clothing, and to the poverty in which she is forced to live. The mother is totally incompetent, sick, and slovenly. This child has many personality difficulties, but all of them are based on home conditions and not on her heart lesion.

CASE 9.—*At ten years.* The first knowledge of heart disease was at six years. She had numerous attacks of chorea. The psychiatrist states, "Average intelligence, guidance problem on account of attentio. getting mechanism. Utilizes cardiac disability as a method for obtaining of a .ention." She was at Caldwell eleven months, having been admitted as Class 11A. She gained 20 pounds in one year. The social service worker reports on admission, "Two years retarded at school, and annoys children in class by actions. One teacher said she was always getting into trouble."

At fifteen years. The patient is a Jewish girl, large for her age, rather attractive looking. Low average intelligence and seventh grade school work is about the limit of her mental ability. She is having considerable difficulty in some of her studies, and is rather embarrassed by the lack of progress in school. She is interested in dramatics and apparently has very little self-consciousness about public appearances. Her social development is perfectly normal. There is no evidence of any social or emotional difficulty on account of her heart disease. When questioned regarding her school standing, she deliberately gave the information that she was one year ahead of her actual grade. She is taking dramatic lessons and is planning for the future on the stage or in radio.

CASE 10.—*At eight years.* With this child the first knowledge of heart disease was at six years. On two separate psychiatric examinations, the child was rated as of low average intelligence, and the second time as a definitely inferior child. She was admitted to Caldwell at eight years and stayed twenty-three months.

During this period she gained 11 pounds. She was rated in class 11B. She had one hospital admission for decompensation. The psychiatrist's examination showed a low average intelligence, and the psychiatrist reports, "I have obtained a rating that I think is entirely unfair. In a test where the child was permitted to work on her own she seemed to show about average intelligence. She seems to go into some sort of a panic when you try to directly ask her a question." There is no direct evidence in this case of any abnormal utilization of her cardiac disability.

At fifteen years. The patient is a fifteen-year-old girl of definitely low mental ability. The younger brother is a low grade moron. The family has been on relief for two years. She takes no active leadership in any activities in school, and presents no problem as long as she is in a protected environment. Her heart disease probably furnishes her with the readily available explanation for all of her inadequacies, and is frequently utilized as such.

CASE 11.—*At eleven years.* The first knowledge of heart disease was at ten years. This child has normal intelligence and presents no particular mental hygiene problem.

At fifteen years. The patient is a well-developed, stolid appearing, Jewish girl with a ready mind and a fair amount of ability. She has a persistent educational drive probably greater than her actual mental attainment. She is in a difficult social position due to religious factors which seem at the present time to be the basis of most of her disturbances. Her attitude toward her heart disease is one of absolute acceptance, with a tendency to ignore all of its implications and possibilities.

CASE 12.—*At eleven years.* The first knowledge of heart disease in the patient was at the age of seven years. The child was very difficult and badly adjusted both at home and in school. The psychiatrist reports, "Superior intelligence, bad home environment, many difficulties on basis of attention-getting mechanism on her heart disease." She stayed at Caldwell one year. She has had two previous attacks of cardiac decompensation.

At sixteen years. The girl is in attendance at high school and is doing reasonably well. She is having a great deal of difficulty in her social adjustment on a basis of a feeling of inferiority about which she definitely complains. She attributes this to the fact that she is not able to dress well or to have the things in her home that most other children have. She shows a definite shyness. Whether this is truly on the basis of the financial position of the family or whether it is due to other causes has not been determined. There is no attempt at the present time to use her cardiac pathology as an escape mechanism. She does better on the personality test than would be expected by the interview.

CASE 13.—*At eleven years.* The first knowledge of heart disease was at six years. There was no hospitalization for decompensation. The psychiatrist reports, "Shows average intelligence with no special mental hygiene problem." She was thirteen months at Caldwell and gained 10 pounds.

At sixteen years. The patient is a rather small, normally developed, Jewish girl with an extremely vivacious and happy personality. She is particularly interested at the present time in high school athletics and athletes. She apparently has a full social life, and in spite of her heart condition takes part in basketball, as a member of an outside team. The child gives the impression of an exceptionally well-adjusted adolescent girl who is having a very good time in everything she does, and to whom the heart lesion means absolutely nothing.

CASE 14.—*At nine years.* The child shows average intelligence but there is definitely bad environment. The psychiatrist reports, "Utilizes sickness as an attention getting mechanism." The father deserted this family when the child was

six months old. The older daughters are now married but for a long time were definite social problems. The child, when she first came under observation at seven years, had very definite adjustment problems both on the basis of the difficult home environment and the possession of sexual knowledge and interest far beyond her age.

At sixteen years. The child is well poised and has made a successful school adjustment. She is apparently developing along perfectly normal lines, and the extra protection that her lesion has given her has very probably been a saving characteristic in the life of this child. Her interests are normal for her age and she shows normal social development. She plans to be a dental assistant. This is possibly due to a long continued hospital contact, but her choice is well reasoned and intelligent, and there is no reason to believe she will not be able to carry it out to a fairly successful conclusion.

CASE 15.—*At eleven years.* The first knowledge of heart disease was at five years. For the last four years before her admission to Caldwell, this child had been completely hospitalized. Her mental hygiene problems are those of long-continued hospitalization.

At sixteen years. The patient is a sixteen-year-old American girl of German parentage, the fourth of five children in a normal middle-class family. They have never been on relief as the father is a skilled laborer and has worked fairly steadily even through the depression. She is very large and has some difficulties due to the fact, as she says, that she is one of the two largest children in the school. She has a definite reading disability even beyond what might be expected with her slightly below average mentality. Her ratings on most of the tests probably are lower than is actually justifiable on account of this reading disability. She is not exceptionally shy, although somewhat retiring, and has only a few close friends. Her heterosexual contacts have not been established and although she is sixteen years old, her reactions are decidedly below her chronologic age. She has the advantage of a home background that is relatively free from overemphasis either on her physical condition or her mental handicaps. She is the only child in the group that is definitely left-handed. On the whole, she has made a reasonable adjustment to her cardiac condition. It is noticeable that the release from gymnasium which she has obtained on the basis of her condition is looked upon as a decided advantage and not a handicap.

CASE 16.—*At eleven years.* This patient was referred from the child Guidance Clinic. The social worker states, "Rather dull, low average type, stumbles over her words while talking." Psychiatrist reports, "Child guidance problem, inferior intelligence, organic handicap."

At sixteen years. The patient is an extremely attractive, vivacious, sixteen-year-old-girl of Italian parentage. She is working in a factory and has made exceptionally good adjustment socially and in her work. She is extremely interested in boys in general, and at the present time, one in particular. Her attitudes on sexual relationships are typical and normal of the age group. Her main resentment at home is against the restrictions of the old-fashioned Italian family which are in this case fairly rigid. However, they are fairly well accepted since they are common in the social group in which she lives. She completely suppresses all knowledge of her cardiac lesion and its possible limitations. The extremely bad showing on the personality test is probably based on her history rather than her actual existing conditions.

CASE 17.—*At eight years.* The psychiatrist reports, "Normal intelligence, no special mental hygiene problem." The child, however, is somewhat immature for her age and shows the effect of an overprotective home environment.

At seventeen years. The patient is a well-developed girl, mixed German and Irish extraction, not quite as self-possessed and poised as most of the children in

this group. She has been fairly successful scholastically and at the present time is working. Her ambitions and plans for the future are practical. Socially, she seems to be making a normal adjustment for her age and social group, and there seem to be no difficulties on the basis of her cardiac pathology.

CASE 18.—*At twelve years.* The first knowledge of heart disease in this girl was at nine years. She was admitted to the hospital in December, 1929, and stayed there for three years. From September 1931 to January 1935, this child alternated between the hospital and the convalescent home at Caldwell. She has had numerous attacks of cardiac decompensation. Since January 1935, she has been at home. The child has a mitral and aortic lesion and blood pressure 190 over 0. She is of superior intelligence, but shows the characteristic dependencies of a child who practically has been brought up in a hospital. The psychiatrist made no special recommendations because prognosis was so bad that it was not thought worth while to attempt any special treatment.

At seventeen years. The girl is well-developed, especially pretty, with red hair and fair skin. She was well poised and very cooperative during the interview. Although a very attractive looking youngster, to the trained eye she shows the marked pulsations of aortic insufficiency. In spite of a very difficult home situation, this child seems to be well adjusted both socially and emotionally.

CASE 19.—*At thirteen years.* The first knowledge of heart disease in this patient was at nine years. There was no history of decompensation. There had been three attacks of rheumatic fever with arthritis and one attack of chorea. The patient stayed at Caldwell three months and gained 10 pounds. This child was admitted on recommendation of the Child Guidance Clinic with the complaint that the child was absolutely unmanageable at home.

At seventeen years. She is an extremely attractive Italian girl, well poised and physically well developed. She is working at the present time in a factory but is anxious to become a dress designer, the handicap being purely financial. She is of better than average mentality and seems extremely well adjusted. The problem of her home is primarily that of a young girl in an Italian family with usual restrictions. It does not seem that there is any special attention paid to her heart condition either by her family or herself. She lives a perfectly normal life, has normal desires and realizations. Her social development is better than average.

CASE 20.—*At eleven years.* The first knowledge of heart disease was at six years. The child was hospitalized for decompensation at seven years. She remained in the hospital five months. At nine years she was again hospitalized, remaining six months. She stayed at Caldwell fourteen months and gained 35 pounds. Previous to admission, this child had spent almost the entire last five years in hospitals. The psychiatrist reports, "Average intelligence with no special mental hygiene problem." The home situation was totally inadequate, her mother having died when the child was about five years of age. The father remarried and died within two years.

At seventeen years. The home conditions of this child are so bad that she was discharged from the institution to a foster home. In the foster home she has made a very desirable social adjustment. She seems to have no real emotional difficulties. This child is a very submissive type of youngster, and has accepted her heart disease without any special disturbance.

CASE 21.—*At eleven years.* The first knowledge of heart disease was at seven years. This child showed all the reactions typical of overprotection and was infantile even beyond what would be expected with a limited intelligence. Psychiatrist reports, "A low average intelligence."

At eighteen years. The patient is a stolid, overdressed, oversophisticated girl, a rather dull normal with only seventh grade schooling. She has made a fairly successful adjustment, making up for her intellectual deficiencies by a fairly attractive physique and a willingness and desire for social contacts. Her comprehension of her disability or own shortcomings is practically nil.

In addition to the data presented above in the summaries of the case histories, two methods of objective testing were employed. These tests were selected because they appeared to have been properly standardized and could give us some method of establishing comparative ratings. Furthermore, they were fairly easy to apply in the age group with which we were dealing. The "Bell Inventory" with its divisions into home, health, social, and emotional adjustment, seemed to be particularly well planned for this work.

TABLE III

RATING ON BELL ADJUSTMENT INVENTORY

CASE NO.	AGE	HOME	HEALTH	SOCIAL	EMOTIONAL
1	12	5	6	10	20
2	13	0	7	17	14
3	13	13	5	13	10
4	--	--	--	--	--
5	13	0	9	8	2
6	13	10	4	13	4
7	14	27	12	18	15
8	14	9	14	18	12
9	14	9	8	5	6
10	15	6	11	20	10
11	15	16	11	11	12
12	16	0	4	14	2
13	16	6	6	6	4
14	16	8	20	15	11
15	16	2	6	16	3
16	16	17	19	14	27
17	--	--	--	--	--
18	17	5	14	16	1
19	17	14	5	8	17
20	17	3	7	10	3
21	18	2	5	4	4

BELL INVENTORY TESTING

As will be seen in Table III, the "Bell Inventory" classification of the home adjustment shows a fairly average distribution. The distribution, if anything, is a little better than would be expected in a normal group from the same economic class that these patients represent. In the section on health inventory, this distribution, representing the personality health factors, shows in 14 out of 19 cases, average or better than average ratings and indicates only a slight increase in health consciousness above the figures for a normal group of this age.

Apparently, from the standpoint of the effect of the chronic illness from which these children suffer on their personalities, this method, as employed, does not indicate any evidence of increasing personality dif-

ficulties on the basis of the cardiac disease. The social rating on the Bell scale is of extreme interest. We are dealing with a group of children with a long-continued disabling condition whose social ratings according to the Bell scale are definitely above average. Of the 21 children under consideration, no single child has fallen below the average rating, and 8 out of the 21 show either good or excellent ratings. On the emotional adjustment, 17 out of the 19 children were average or better. Only 1 case, No. 16, rated very unsatisfactory. This rating, confirmed by the Thurstone Personality Schedule, can be very readily

TABLE IV

CLASSIFICATION OF RATINGS ON THE BELL INVENTORY

(CLASSIFICATION NUMBERS)

Home

Rating	*Group*	*No. of Cases*
0—2	Excellent	5
3—5	Good	3
6—13	Average	7
14—20	Unsatisfactory	3
20—over	Very unsatisfactory	1

Health

Rating	*Group*	*No. of Cases*
0—1	Excellent	1
2—4	Good	2
5—11	Average	11
12—16	Unsatisfactory	3
16—over	Very unsatisfactory	2

Social

Rating	*Group*	*No. of Cases*
0—4	Excellent	1
5—10	Good	7
11—21	Average	11
22—30	Unsatisfactory	0
30—over	Very unsatisfactory	0

Emotional

Rating	*Group*	*No. of Cases*
0—3	Excellent	3
4—8	Good	6
9—18	Average	8
18—24	Unsatisfactory	1
24—over	Very unsatisfactory	1

explained if the past history of this child is understood and evaluated. The writer and his associates felt during the examinations that this rating was rather an expression of historical facts than of present emotional difficulties.

THURSTONE PERSONALITY TESTS

The Thurstone Personality Schedule which was the other objective test selected for this group shows a similar high distribution. Fifteen out of 19 children show average or better. Only 3 are emotionally

maladjusted, and only one Case, No. 16, to which reference was made above, shows the need of any special therapy on the test.

From the mass of material gathered at the interviews, we have attempted to tabulate some of the data in a form that would make it easier

TABLE V

RATING ON THURSTONE PERSONALITY SCHEDULE

CASE NO.	AGE	RATING	CASE NO.	AGE	RATING
1	12	57	12	16	22
2	13	43	13	16	20
3	13	37	14	16	52
4	13	none	15	16	24
5	13	24	16	17	98
6	13	24	17	17	none
7	14	60	18	17	28
8	14	76	19	17	54
9	14	22	20	17	27
10	15	45	21	18	15
11	15	44			

TABLE VI

CLASSIFICATION OF RATINGS ON THURSTONE PERSONALITY SCHEDULE

The division into groups according to Thurstone is as follows:

Ratings	*Group*	*No. of cases*
0—14	Exceptionally well adjusted	0
15—29	Well adjusted	9
30—59	Average	6
60—79	Emotionally maladjusted	3
80—over	Psychiatric admission note	1

to visualize the actual development of these children. One of the factors that interested us was the attitude of the child to her heart condition and the question of whether or not there was any direct relationship between the resentment felt at the disability and the physical extent of the disability. A study of Table VII shows that apparently this

TABLE VII

CASE NO.	DEGREE OF DISABILITY	ADMITTED	RESENTED	CASE NO.	DEGREE OF DISABILITY	ADMITTED	RESENTED
1	1	yes	no	12	1	no	no
2	1	no	no	13	2	yes	no
3	1	yes	no	14	1	no	no
4	1	yes	no	15	1	no	no
5	1	no	no	16	1	no	no
6	2	yes	no	17	2	yes	no
7	1	no	no	18	1	yes	no
8	1	no	no	19	1	yes	no
9	1	no	no	20	2	yes	no
10	1	yes	no	21	1	yes	no
11	1	yes	no				

is not true. In determining the degree of disability for the purpose of this table, Class 1 represents children who were able to take part in

practically all normal activities and had, therefore, very little restriction in their ordinary contacts. Those classified as Class 2 were children for whom it was impossible to carry out the normal play activities of this age group with anything like the efficiency that the average youngster shows. It will be noted that all the children in Class 2 admit definite disability and that very many of the children in Class 1 also admit their cardiac disability. There were 9 cases out of the 21 that refused to admit any disability at all. It was impossible to elicit from any of the children any statement that would tend to show an attitude of resentfulness toward their disability.

One other table has been added which presents an interesting view of the reactions of these children to their heart condition. All of these children are excused from attendance in gymnasium in the school. It will be noted that in Case 15 the child tells her classmates, with evi-

TABLE VIII

GYMNASIUM EXCUSES

1. Special cardiac class	12. Does not tell
2. Tells reason	13. Tells reason
3. Tells reason	14. Tells reason
4. Tells reason	15. Tells with pride
5. Tells reason	16. Does not tell
6. Tells reason	17. Does not tell
7. Tells reason	18. Tells reason
8. Does not tell	19. Does not tell
9. Tells reason	20. Tells reason
10. Tells reason	21. Tells reason
11. Tells reason	

dences of pride, that she does not have to take gymnasium because she has a heart lesion. Apparently to this child, this condition seemed to place her in a favored class. Out of the 21 cases studied, case No. 1 being in a cardiac class, of course would find it impossible to hide the reason for her gymnasium excuse. Of the others, only 5 out of the 20 have any reluctance at all about telling their playfellows the reason for their excuses from gymnasium. All the other children apparently admit the reason without any special feeling of incompetency.

The characteristic statement made by these children in this connection is: "Oh, yes, I am excused from gymnasium on account of my heart, but very many of my friends are excused from gymnasium. Some of them have appendicitis, and some of them have other conditions."

There does not seem to be any special feeling of disability connected with gymnasium excuses in the public schools in our city.

SOCIAL ACTIVITIES

As another check on the social development of these youngsters, it was interesting to see how many of them actually took an active part in the social life of the school and their community. Of course, as small

a group as this does not lend itself to statistical analysis, but even a cursory glance over Table IX which shows the activities of these children in leadership in schools, clubs, etc., furnishes a very interesting

TABLE IX

CLUB ACTIVITIES

1.	0
2.	President of school council
3.	0
4.	0
5.	0
6.	Secretary of current events
7.	Secretary of social club
8.	0
9.	Cheerleader, chairman of program and entertainment committees
10.	Treasurer of social club, President of dramatic club, solo singer
11.	0
12.	0
13.	Editor of school paper
14.	Glee club, solo parts, class secretary, chairman current events
15.	0
16.	Vice president, treasurer social club
17.	President social club
18.	Class president
19.	0
20.	Secretary social club
21.	President social club

commentary on their social development. Certainly, this group as shown by the table is more active in the social life available than the average child could possibly be.

In Table X, an effort was made to find out what the reaction of this group was to public appearances. The assumption was made that if a child suffered from a definite feeling of inferiority she would be very unlikely in the ordinary schools of the community to attempt performance in public. Nine out of the 19 children examined definitely perform in public, and this certainly may be accepted as evidence of the lack of any general tendency in the group to withdraw. We have classified this reaction to public appearances according to 4 groups.

TABLE X

PUBLIC APPEARANCES

CASE NO.	CLASSIFICATION NO.*	CASE NO.	CLASSIFICATION NO.
1	1	11	1
2	3	12	4
3	1	13	3
4	2	14	3
5	1	15	3
6	4	16	2
7	3	17	3
8	3	18	1
9	3	19	2
10	4	20	2
		21	3

*1, Dislikes; 2, likes but bashful; 3, performs; 4, indifferent.

1. The child who definitely dislikes to make a public appearance. 2. The child who would like to make the appearance but feels a certain sense of insecurity and bashfulness. 3. The child who actually performs in public. 4. The child who is entirely indifferent, neither desiring to perform in public nor being especially distressed by the necessity when it arises.

As will be seen in Table X, only 5 of these children were classified as group 1 definitely showing some withdrawal tendency; 4 as group 2 which may be taken as indicating children in whom some inferiority complex exists; 9 as Group 3 children who are actually making some type of public appearance; and 3 as Group 4 children who although occasionally making a public appearance, are not particularly interested in this sort of thing. Although the group is small, the distribution is extreme enough to make one feel that at least for the group as a whole there has been no definite disturbance that would interfere with their making public appearances.

One other very interesting observation has been that where a child suffers from a serious ailment, there is usually a tendency on the part of the family to overcompensate for it. When there are other children in the family, this very frequently gives rise to a very unpleasant and sometimes a serious situation. Sibling rivalry is very hard to ascertain in an interview, but where the entire family is known, as is the case with the group under consideration, very frequently evidences of sibling rivalry may be obtained from the other children. Table XI gives a classification of these cases which we believe to be fairly accurate.

TABLE XI

SIBLING RIVALRY

CASE NO.	CLASSIFICATION NO.*	CASE NO.	CLASSIFICATION NO.
1	X	13	1
2	0	14	2
3	1	15	0
4	1	16	0
5	1	17	0
6	0	18	1
7	1	19	2
8	0	20	2, disbelieves other child's illness
9	0		
10	1	21	0
11	0		
12	2		

*X, no sibling; 1, normal; 2, excessive; 0, nothing.

Only 3 of these children show excessive rivalry at the present time. This was a very definite part of the attitude of very many of these children when first seen. In Case No. 20, the sibling rivalry is so intense that although the other child really is seriously ill, this child is unwilling to admit the possibility of any real illness.

VOCATIONAL INTERESTS

Most of these children are approaching, or have already entered into the age group where definite vocational guidance is necessary. A tabulation was made of the vocational interests and choices in Table XII.

On the whole, the vocational choice is very similar to that of any group of girls of like age in the economic and social status from which these children were drawn. There is, however, a preponderance of serv-

TABLE XII

VOCATIONAL CHOICE

1. 0	11. 0
2. 0	12. Nurse
3. 0	13. Secretary
4. Secretary	14. Secretary
5. Secretary	15. 0
6. Nurse	16. Nurse, dietitian
7. Dress designing	17. Secretary
8. Factory hand	18. Nurse
9. Commercial art	19. 0
10. Radio acting	20. Nurse, technician
	21. Factory hand

ice vocational choices; nurses, dietitians, and technicians. On further questioning most of the girls seem to have been influenced primarily by the fact that for so great a part of their lives, they have been in contact with hospitals and hospital personnel. It is only natural, therefore, to expect that many of them will set up as their own ideal some individual within the group with which they have been in close association.

Some very interesting information was obtained on the problem of heterosexual contacts. These girls ranging from twelve to eighteen years are in an age group where the development of heterosexual interests is an extremely important factor in evaluating their general development. Information of this type was obtained with unusual facility because the interviewer had stood for many years in loco parentis to the children. As a matter of fact, his professional prestige and their own long history of dependencies made them especially confiding. We have attempted in Table XIII to classify these contacts in five groups. Group 1 where heterosexual contacts are not desired were girls that exhibited the ordinary attitudes of girls about nine or ten years of age. Some of the characteristic statements in this class were, "I don't like any boys," or "Boys in my class are fresh, when the teacher talks to them, they think they are smart." "Parties are better when there are no boys there, because they make too much noise." "We are much better off without boys. Our science teacher thinks so." "I don't like to go out with boys yet." "I don't think they notice your clothes but the girls do."

TABLE XIII

HETEROSEXUAL CONTACTS

CASE NO.	PRESENT AGE	CLASSIFICATION NO.*	CASE NO.	PRESENT AGE	CLASSIFICATION NO.*
1	12	4	11	15	2
2	13	1	12	16	1
3	13	1	13	16	4
4	13	3	14	16	4
5	13	1	15	16	3
6	13	2	16	17	5
7	14	1	17	17	4
8	14	3	18	17	4
9	14	4	19	17	4
10	15	1	20	17	3
			21	18	4

*1, Not desired; 2, bashful but desired; 3, accepted but reticent; 4, frank; 5, adult.

In Group 2, we took for classification what is apparently a very frequent attitude in early adolescence. The type of answer that was obtained in the interview was something along these lines: "I don't care for boys very much." "I don't know very many boys, sometimes I walk to school with a boy." "I feel sort of self-conscious with boys at a party. I guess I am bashful. I guess they know it too. They tease me and say I am bashful."

In the third group we have attempted to include those who have accepted and established definite boy and girl relationships, but still at the same time are reticent when questioned concerning these relationships. Ordinarily, this makes up a very large group, but in the interviews as conducted, there are only 4 cases that fall definitely into this classification, and from whom it was impossible to get any definite statement as to their attitude toward boys. Characteristic statements in this group are such as: "I don't think boys spoil a party, but I don't care whether they are there or not." "I know some boys but I don't go to their houses." "My girl friend has a boy friend but I don't have any special boy friend." "Sometimes you have more fun when boys are there, and sometimes more fun with girls."

Group 4 is the largest group among the older girls in the series. Here their very definite interest in boys is manifest, but it is an interest in groups of boys rather than single individuals. Most of these children state that they like mixed parties rather than parties with girls alone, and they like to go out in crowds with boys and girls. They all energetically deny interest in any special boy, and apparently this is true as most of the contacts seem to be those of groups of girls with groups of boys rather than individual contacts.

There is really only one case in this whole series classified as 5, the adult type of relationship where a definite boy and girl friendship has been established with the idea of a future marriage. This type of relationship of course, is completely out of the range of adolescence.

INFLUENCE OF PHYSICAL DISABILITY

There has been a large amount of investigation done on the effect on children of the presence of visible physical deformities. Common experience has shown that the sufferer from infantile paralysis with the lame leg; the child with a harelip; the child with a noticeable birth mark, have all tended toward a psychic disturbance based on the physical deformity itself. Whether the knowledge in the child of the extent of the physical deformity, or the reaction of the community to this deformity is a primary factor in these psychic disturbances has not been evaluated. Oscar M. Sullivan[3] says:

"It is quite essential that even in the earliest years the right principles for dealing with the handicapped condition as it affects the child shall be understood by the parents and by the others around him. Otherwise in the pre-school period, or in the out-of-school time, the child may receive such a conditioning that he can never face the world adequately and play a self-contained individual's part in it. . . . "

In spite of the fact that this writer advises the development of compensatory accomplishments, he states in another part of the same paper this recommendation:

"A second important recommendation of the mental hygiene advisers is so to train handicapped children that they avoid the escape habit. They should know from the beginning that they will have to face realities. Pity and coddling have no place in the treatment of the handicapped child . . . . "

It is worthy of note that a physical deformity in itself is not always the cause of psychic disturbance. The saber scar of the dueling student in a German university has a very close resemblance to the facial deformity following an automobile accident; but one would never compare the feeling of pride that accompanies one with the distress and the desire to withdraw that is the result of the other. Similarly, in our eyes, the harelip is no greater deformity than the large plate lips of the Ubangi maiden which in her social group is a sign of great beauty. The reaction of the social group to these voluntarily inflicted deformities always contains within it this element. How true this is is still further brought out by the general concept in poetry and literature that a deformed body contains a deformed mind; that the hunchback and dwarf while jesters for a court had always to be reckoned with as treacherous, antisocial, and destructive. This viewpoint we believe is sometimes not fully appreciated. R. A. Jefferson[4] states:

" . . . Whereas the visibility of the one type defies secrecy and promotes a compensatory psychobiological striving while the world makes allowances, the hiddenness of the latter, with the secrecy and shame which so frequently accompanies, makes of social adaptation a doubly difficult task. . . . "

We do not believe that this is true, because in our experience, the social adaptability of these children when proper mental hygiene pro-

cedures has been instituted, is very much greater than that which may be hoped for in any group of visibly physically deformed children. In support of this contention, Brenton M. Hamil,[5] states as follows:

> " . . . Much is continually being said about the inferiority feelings which develop in an individual as a direct expression of his feelings of incapacity because of a physical abnormality. This may be true in rationalizing adults. . . . The abnormality in itself is not the greatest handicap. The emotional conflicts which result because of parental or social attitudes regarding these abnormalities are of most importance. A person who is constantly hearing some kind of reference to his abnormality or who is constantly having things done for him which he is capable of doing with some degree of efficiency himself, will either show a quite natural reaction, revolt, or he will take advantage of the situation to get unhealthy recognition because of his physical handicap. Constant attention to a handicap, whether it be in the form of nicknames relating to it, or whether it be in the form of sympathy or special privileges because of it, will usually become a type of nagging in the interpretation and emotional response of the afflicted. Children with speech difficulties may withdraw because of revolt at being unable to make themselves understood. The cripple may withdraw because of revolt at being unable to exert his ego in play competition with normal children. The child who has undetected faulty vision or color blindness, or the child who unknowingly does not hear well may withdraw because his sincere attempts in his best possible accomplishments are looked upon by the teacher or parents as lack of effort. The other most common reactions in such cases are regression, or temper tantrums and fighting.
>
> A child has an ability for interpretation of the attitudes of members of his environment . . . "

The idea is widely held that the development of a child should be considered as a unitary thing with the realization that in order to have normal and satisfactory adjustment, all of the factors entering must be normal. In this view, a sound mind in a sound body is the ideal, and the development of a sound emotional and social being in the absence of a well body has been denied at least by implication. In the handling of these children very many workers have stressed the importance of establishing compensatory mechanisms for the physical deformity. The ability of the child to develop some special talent as a compensation for its general physical inability has in my opinion, two very definite disadvantages. The first is that very frequently the ability developed is of no social importance, and secondly, very many children do not possess even the latent qualities that are necessary for the development of outstanding perfection in any field. There is also another very definite weakness in a policy of compensation. When the child ultimately realizes, under some special stress, that these compensatory activities are not real, the damage to his self-esteem and to his personality, is likely to be very severe.

In this group we have children who have a physical deformity and handicap. The deformity is not visible, and although the child from a very early age has knowledge of this deformity and the limitations

which it imposes, in some instances even greater than the limitations imposed by visible physical deformities, it has been our observation that the presence of these handicaps has not caused any marked deviation from the standards of ordinary conduct or any disturbance in the development of normal social relationships. The data that we have presented in the tables, particularly the factor of social adjustment in the Bell Inventory where no single child in the whole group has fallen below an average social rating, is certain indication of the ability of these children, under proper guidance, to develop perfectly normal social contacts. If this is true, the primary cause of psychic disturbance is not the knowledge of the handicap by the child itself, but rather in the reaction of the child to evidences of recognition of this handicap by the community in which it lives. As a matter of fact, in these particular children the disease does not detract from their attractiveness but rather enhances it. The high color of the person with mitral valvular disease is likely to be considered a very attractive feature, and the large moist eyes of the patient with chronic valvular disease in reality lend a certain type of beauty to the features. To the untrained observer, the child that has attained a physical adjustment so as to be able to carry on most of the ordinary procedures, offers a picture of perfect health. We believe that in the type of treatment offered, one very essential factor enters that to a great extent may contribute to the successful adjustment that these children make. It will be noted that with the separation of the child from the family for a period of over one year, the element of overprotectiveness in the home has been definitely minimized. It is also an interesting observation that the sense of guilt felt by the parent in these cases has to a great extent been dissipated, due to their contact with many children of the same type in other families, and their contacts with parents of other children with heart disease. This sense of parental guilt which is always a serious factor in the management of sick children, particularly children with chronic or incurable illnesses, is often aggravated by the method in which the history of the case is obtained.

When one remembers that the parents start with a sense of guilt and then everyone maybe of a dozen people, physicians, social workers, psychiatrists, etc., in taking the history lays great stress upon the hereditary factors this sense of guilt is greatly increased. They go into great lengths as to whether the father, mother, grandparents, uncles, or aunts, have ever had rheumatism or heart disease, and the sense of responsibility for the condition continues to grow. In our own work, we have made it a special point that in obtaining the familial history of the condition, care be exercised so as not to create the impression that this is a disease visited upon the children even to the third generation.

These children, removed from homes ordinarily on the poverty level, with improper food, with improper facilities, with worried and dis-

tracted parents, are placed in an environment where all of these factors are removed. A feeling of complete security is established by the institutional personnel. Although when the children are first admitted and during the following period of observation the restrictions are very severe, it has been our policy that as soon as it was medically permissible to permit the child up, the assumption was made that the child was perfectly normal and able to do everything that it pleased. It is surprising how easy it is to instill a feeling of complete adequacy at the same time as they are being taught the necessity of certain restrictions and control. Our policy in the institution, briefly, has been to keep the child in bed as much of the day as was necessary, but under no conditions to permit interference with the child's activity in the time that she was permitted up. We found that if this time was carefully apportioned, and the child was constantly watched, there was no danger to the child physically from this procedure.

There is no question in our minds that from the standpoint of the development of healthy mental attitudes, this is the only procedure that will not create a constant feeling of physical inefficiency. A study of the cases offered will show that once these habits of control of physical activity, within the limits set by the child's own condition and recognized by her, have been established, these procedures can then be carried out by the child unsupervised without creating conflicts and dissatisfactions. The acceptance of the idea of the possibility of cardiac death in other children combined with a real ability to ignore its application to oneself has been characteristically present in the interviews. This definite feeling of euphoria that is so characteristic in tuberculosis also seems present in heart disease. When these children were questioned regarding their reactions to the knowledge of the death of other members of this group, the responses although formally satisfactory revealed a total lack of emotional involvement in the death of another child. This was particularly noticeable in view of the fact that the girls had lived together in a relatively small community group over a fairly long period. One or two of the children did say that when very sick, they felt a fear of death but now that their condition had improved, although they realized that other children who had seemed perfectly well had died of heart disease, this did not apply to them. This protective mechanism apparently is of great value in avoiding emotional disturbances on a basis of their cardiac pathology.

In the choice of vocations, as will be seen in Table XII, a very large percentage of the group have expressed the desire of entering into the field of nursing or one of its allied branches. This is to be expected as all of these children have had rather extensive hospital experience, and naturally many of their ideals have been determined by their environment. When these children were informed that nursing opportunities

were closed to them on account of their heart condition, the reaction always indicated that this had been considered if not directly, at least subconsciously, that they were prepared to obtain the same type of satisfaction in some available form when the opportunity to do bedside nursing was denied. The large percentage of the children who plan to do secretarial type of work is not based on the feeling of physical inferiority, but is rather approximately the percentage that would select this type of work in any group from the same social and economic background.

We have presented here a fairly large group of girls with rheumatic heart disease who have been under intensive observation for a relatively long period of time. We find that although many of these children come to us with definite social and emotional maladjustments, under reasonable care, most of these problems may be solved.

The two primary factors that enter into these problems are the parents' guilt complex, and the child's utilization of its organic defect for purposes either of attention-getting or for the development of her own feeling of security. The separation of the child from the home makes it possible to establish healthy normal attitudes both in the child toward the organic defect, and in the members of the household toward their sense of responsibility. This is very much easier with children who have no visible deformity than it could possibly be in children where the deformity is always a cause of comment in the community.

On account of the small number of children involved, none of this material is suitable for statistical analysis, and therefore, is presented only in tabular form.

SUMMARY

For the past fifteen years we have had an opportunity to study a large group of girls with rheumatic heart disease. In addition to the physical problems arising from their cardiac disease, the emotional and social development of these children offers an interesting field for study.

A group of 21 girls, who at the present time range between twelve and eighteen years of age, were selected for study. The age of discovery of the heart disease varied from two to ten years, with an average age of seven and one-half years. All of these children had a residential period at the Theresa Grotto Residential School for Cardiac Children at Caldwell, N. J. The average length of this residential period was fourteen months. The average age on admission to the cardiac home was eight and one-half years. The average age of the 21 children in the group studied at the time of the final study was fifteen and one-half years. Complete social service and psychiatric studies were made on all of these children on admission. These preliminary studies to which were added complete long-time observation and control, which included physical,

economic, and psychiatric details, furnished the background for the present study. The time interval between the preliminary studies and a final survey varied from two to eleven years.

Two methods of obtaining the data were utilized. The first was a critical study of all the material in the files over the entire period during which the child had been under observation, checked and correlated with a final psychiatric study by the interview method on each child. These studies were felt to be of particular value as these children had been under the personal control and medical supervision of the observer for periods ranging from three to fifteen years. The second method utilized was the testing of the entire group by the "Bell Adjustment Inventory" and the "Thurstone Personality Schedule."

These objective tests gave ratings that corresponded very well with the ratings given by the first method, and may be summarized in the following conclusions:

1. Although the child from a very early age has knowledge of the disability and the limitations which it imposes, in some instances even greater than the limitations imposed by visible physical deformities, it has been our observation that the presence of these handicaps has not caused any marked deviation from the standards of ordinary conduct or any disturbance in the development of normal social relationships.

2. That one of the important factors in the development of emotional and social difficulties in these children has been the sense of guilt of the parents.

3. That another major factor in the development of these difficulties has been the attitude of overprotectiveness in the home based on the fear of the cardiac disease.

4. The utilization of a residential school for cardiac children offers an opportunity for the establishment of a successful mental hygiene program and leads to the disappearance in most of these children of undesirable mechanisms established in the home.

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Critical Review

THE NATURE OF THE AMERICAN DIET

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EARLIER reviews in this series have discussed the nature of nutritional needs of the human organism, and the manner in which they may be met.[1] Evidence was presented to establish the prevalence of suboptimal states of nutrition. One must infer from the numerous studies in this field of investigation that a large proportion of the people of this country are handicapping themselves through the inadequacy of their diets. The extent and significance of this status is not appreciated by the population at large nor by many of those concerned with problems of health. This review is directed toward analyzing some data concerning food consumption in this country and comparing the findings with dietary standards designed for optimum nutrition.

In preparing this presentation, publications by various divisions of the federal and state governments have been used freely. The recently published reports of the Committee on Foods of the League of Nations summarize in themselves most of the salient points brought out in this review and have been of great assistance in its preparation.[2] Some of the data and information have been gained from unpublished reports or from personal correspondence with directors of experimental stations and with others who have studied the problem of nutrition in the field. The author gratefully acknowledges the excellent cooperation and assistance of these agents.

Several methods of approach have been used in studying the nature of food consumption. By correlating the number of people with the data regarding production, import, and export of various commodities, apparent per capita consumption may be computed. Surveys of foods purchased or consumed in sample areas may be taken as representative of the area as a whole. Individual variation in food habits as compared with the community as a whole may offer an index of the degree of uniformity of nutritional practices. Data so obtained may be studied in terms of geographic locality, occupation, economic and social level, age of the constituents of the population, race, size of family, or other constants. Each of these methods is subject to error in compilation of data and of interpretation. However, discrepancies lose significance when the same qualitative conclusions are reached through studies conducted in different sections of the country, by independent investigative personnel, using diverse methods of attack. The massed statistics do not offer strictly quantitative information, yet they indicate the prevalence of grossly deficient diets, and even greater prevalence of suboptimal states.

A high degree of correlation may be demonstrated between the adequacy of diet and many constants in the manner of life of the

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individual or the community. The lower the expenditure for food, the greater the likelihood of deficiency; yet in every level of outlay for food, much improvement could be accomplished through more intelligent choice of foods. Suitable diets are favored through home production of the necessary components; however but few areas use their facilities efficiently to insure adequate seasonal or year-around supplies of certain foods. Studies of production show that the supply of some essential foodstuffs must be increased considerably if the average need for such commodities is to be met. In the upper economic brackets, the per capita consumption of necessary foodstuffs falls significantly below a desirable level. Probably the first step necessary for the betterment of the nutritional state is to make the people aware of the advantages of optimal nutrition in contradistinction to maintenance or subsistence levels.

STANDARDS FOR NORMAL NUTRITION

Factors needed for nutrition include the following: biologically valuable protein; the minerals which enter into the composition of the tissues or which are used in metabolism; the various vitamins; sources of energy. The latter may be supplied as carbohydrate, protein, or fat. Qualitatively, nutritional needs are similar at all ages; quantitatively, they vary both as to the total and as to the amount of individual constituents. During the period of growth the requirement for proteins and structural minerals is relatively or absolutely greater than in the adult. In the latter, moreover, the requirements for replacement are greater than is generally recognized. During the period of early maturity, needs may continue at levels approximating those of active growth if optimum nutrition has not obtained during the earlier years. The quantitative need for some factors will vary not only with age, but also with the nature of the occupation, geographic location, and other constants. Some data have been expressed in terms of the adult male unit, on the premise that requirements for the remainder of the population are aliquot proportions of this unit. Such data may be misconstrued as applied to the child, especially as regards protein and bone-building minerals, since the requirement of the child is not a linear function of that of the adult. This is particularly important in evaluating the consumption of milk, eggs, and meat.

Foodstuffs vary greatly in their content of nutritional essentials. They may be characterized roughly into two groups, those which offer appreciable concentrations of minerals, vitamins, and first-grade proteins and those which are principally valuable as sources of energy. The first group includes foods such as milk and its products, eggs, fruits, vegetables, fish liver oils, fresh meat products. The second includes some articles which have certain nutritional virtues other than their calorie content, but which for various reasons are less valuable than other forms of foods. Examples include the starches, sugars, and most fats; the highly milled cereals are included with the starches in this category. The foods in the first group are often designated as protective foods because of their dependability in completing the quality of the diet. Whereas inadequacy of calories is encountered in the lower economic levels of some regions, this is far less common than deficiency in protective foods. From the monetary

standpoint, the nonprotective starches, sweets, and fats are the cheapest sources of energy, whereas meat products are among the most expensive. Cereals in their native form have nutritive properties sufficient to rank them as protective foods; as consumed, however, most of their valuable constituents have been removed or destroyed in the processing necessary to insure keeping qualities or to enhance their appearance. The protein of legumes and of some cereals, while noteworthy in amount, is less available for tissue building than that from meat or milk. When supplemented with liberal amounts of milk, the quality of cereal protein is assured. Unmilled cereals constitute a valuable source of iron, a dietary essential which is lacking in some areas. However, Sherman has pointed out that the increased use of cereals usually results in a lessened intake of calcium and of vitamins A, C and G.[3]

Sherman states that the American dietary as a whole tends to supply an excess of protein, but insufficient calcium, and that, whereas proof is less positive, there is reason to believe that a large proportion of American families are underinsured as to vitamins A, C, and G.[4] His observations concerning protein apply to the adult rather than to the child; on theoretical as well as practical grounds, there is reason to believe that the diet of the child is frequently deficient in protein. The League of Nations Committee emphasizes the need for supplementary vitamin D because of the very limited amounts of this vitamin in foods commonly eaten and because exposure to sunlight is often inadequate.

In assessing the quality of diets, various levels of nutrition must be recognized. A publication of the Department of Agriculture offers diets designed to meet different degrees of availability of foodstuffs.[5] The first of these will supply all essentials in liberal amounts and assure the optimum state of nutrition. The second is adequate, but offers less margin of safety against deficiency. The third is of minimum adequacy; it barely meets nutritional needs and does not provide for much storage nor for unusual needs. The fourth is designed for use in nutritional emergencies; not with the idea that it meets nutritional needs, but with the hope that its use will lessen the inadequacy which would result from unguided use of food at times when allowances lie below the minimal level. Even though such diets are not recommended for continuous use because of their inadequacy, they are superior in quality to those commonly used in some marginal groups of our population.

In outlining desirable nutritional practices, the optimal diet should be the objective; it should be one which will supply everything which will contribute toward the achievement of radiant health and normal development. Several authorities have published such diet lists for the various ages of childhood and for the adult. These are in general agreement that the child should receive the following each day: one quart of milk; one egg; two or more liberal servings of vegetables, one of which should be of the pigmented variety, and preferably one should be eaten raw; similar amounts of fruit, part of which should be fresh, preferably raw; liberal amounts of butter; fresh lean meat or fish once a day, if possible; cereal products, sweets, and fats in amounts sufficient to complete the diet, but not to replace any of the

foods specified in the foregoing. This agrees essentially with the recommendations of Mrs. Rose,[6] those of the Committee on Nutrition of the League of Nations, and those of the Department of Agriculture of the United States. The diet advocated by the Department of Pediatrics of the University of Iowa for the control of tooth decay is similar to these others, but it includes in addition a teaspoonful of cod liver oil daily, throughout the year.[7] In the minimal and emergency diet recommendations of the Department of Agriculture, the level of milk intake is maintained at 1½ and 1 pint a day, respectively. To meet the economic need, larger allowances of legumes, dried fruits and cereals are suggested, with some reduction in the amounts of lean meat, fresh fruits and vegetables, and eggs. In each of the diets cited in the foregoing, preponderant use of protective foods will be noted; they supply from 40 to 77½ per cent of the total calories. In contrast to these values the diets employed in 224 American families, as analyzed by Sherman, offered only 20 to 30 per cent of the calories as protective foods.[8]

In evaluating the diet practices of a community it is much easier to detect and define trends than to determine with accuracy the exact intake of an individual or of a community. Marked differences exist from family to family; food use varies with the season of the year and with the financial status. Conclusions may be directed toward certain aspects of the diet or toward the status of nutrition as a whole. One may consider individual variations, or the general condition within the community. To simplify these problems in this review, attention has been directed toward the degree of consumption of milk, eggs, meat, vegetables and fruits as an index of the use of protective foods, and of sugar and cereal products, representative of the less valuable foods.

CONSUMPTION OF MILK

It is necessary to distinguish between data pertaining to the use of total milk products and those concerned with the consumption of milk and cream. In the manufacture of butter, which accounts for about a third of milk production, the protein and mineral content remain in the buttermilk. Whereas some of this will be ingested as cheese, the average consumption of the latter is not great enough (4 to 5½ pounds per year per capita) to represent much of the milk diverted for buttermaking. The use of gross figures has led in some instances to the apparent use of milk in amounts considerably greater than actually consumed. Wherever possible, the data quoted in the discussion to follow include only milk or cream used as such or as ingredients in other foods.

The gross daily milk production in this country in 1934 averaged 98,940 million pounds.[9] If prorated among the population of the United States, this would allow somewhat more than 0.8 pint per capita.[10] Of the total, 12,008 million pounds were consumed as milk or cream on the farm where it was produced. In addition, about 60 per cent of this amount was retailed by the producer in adjacent areas. The remainder was used for buttermaking on farms, fed to calves, skimmed or separated for butterfat, or sold at wholesale. Prorating that consumed on the farms, the allowance per capita of the inhabitants of rural areas is 0.57 pint. When the consumption and

production are considered regionally, the average obtained varies from a low of 0.36 pint per capita in the North Atlantic states to a high of 1.06 pints in the west North Central region. These amounts may be augmented slightly through the retailing of milk in the rural areas, but in general the evaluation probably is fairly correct. Moreover, it is in fair accord with the reports from various state authorities as to observed average consumption.

Data for urban consumption of milk are available through the results of numerous local surveys. In Baltimore the average daily per capita consumption in the higher income district was 0.874 pint, as compared with 0.697 pint in the lower income area.[11] In Philadelphia from an official survey including 3,413 families, the average was 0.65 pint.[12] A house-to-house survey in Burlington, Vt., showed that the younger children received more milk than those who were older, the average daily intake ranging from 1.19 pints to 0.41 pint.[13] In Richmond, Va., the average consumption was calculated to be 0.414 pint daily, as compared with 0.741 pint in New York City.[14] In New Hampshire, eight cities between 12,500 and 77,000 population reported average consumption varying from 0.71 to 1.12 pints.[15] In several large cities on the Pacific coast, the average milk consumption was from 5 to 6 pints per week per capita (0.7 to 0.85 pint).[16] In southern industrial districts, the range was from 3 to 8 pints per week per capita (0.4 to 1.1 pints).[16]

When individual variation from the local averages is studied, a better picture of the status is obtained. Thus, in a study of all the children of preschool age (over 6,000 children) at Gary, Ind., it was reported that 57 per cent had no milk on the day of the survey, and that only 19 per cent had received a pint or more. In the highest income group 38.5 per cent had received no milk.[17] In a Kentucky survey it was reported that milk consumption averaged almost a pint a day, yet 28 per cent of the children received less than that amount.[18] In a Virginia survey it is stated that 40 per cent of a group of children of preschool age did not receive milk, and that of the school age group only 32 per cent received as much as a pint a day.[19] In Texas only 28 per cent of a group of 993 children received as much as three cups of milk a day.[20] In Alabama not more than 50 to 60 per cent of the farm families studied produced enough milk for their own use; among the negro farmers the condition was still less favorable.[21] In village studies in Maine it was estimated that children of preschool age averaged 2.7 cups, school children from 1.7 to 2.4 cups per day.[22] In two small towns in Massachusetts, one located in a dairy area and the other not, 64 per cent of the children in the former received a quart of milk daily, whereas only 16 per cent in the latter city used that amount.[23] In 895 farm homes in New Hampshire, 73 per cent of the households owned cows and averaged 0.9 quart consumption per capita per day. The remainder of the families, however, used but little milk.[24] In South Carolina 10 per cent of the rural population are said to have no cows and to purchase almost no milk. Of the 47 per cent who had but one cow, no provision was made for the family's milk supply while the cow was dry.[25]

From the foregoing, it is evident that in most regions, a varying proportion of the children may receive a desirable amount of milk.

At the same time, there is as large or a much larger number whose milk allowance is decidedly below the amount necessary for suitable nutrition.

To appreciate the need for stress on the level of milk consumption for the child, it is necessary to review his needs for protein, calcium, and phosphorus, and to consider the potential food sources of these three essentials. According to accepted standards, the child needs a gram of protein per pound of his proper body weight each day, or about 70 grams for a child of ten years. A quart of milk will supply half of this amount. An average serving of lean meat will furnish from 12 to 18 grams of protein; an egg, 6 grams; a large dish of oatmeal, about 4 grams; three slices of bread, about 3 grams. The total protein equivalence of these foods will barely meet the predicted need. If the milk allowance is reduced to a pint, it will require an additional liberal serving of lean meat to replace its protein value. If no milk is used, protein deficiency seems inevitable. In view of the ease of ingestion and the low cost of protein in the form of milk, its advantages seem obvious. But milk offers other advantages as well. The calcium need of the child is estimated at a gram a day; this amount is needed to permit the calcification of the hard tissues to keep pace with their growth in volume. A quart of milk a day will supply this amount in a readily usable form, together with a desirable amount of phosphorus. The calcium content of lean meat is negligible.[26] Whereas some other foods may be used as a source of part of the calcium, their concentration of lime salts is such that a disproportionately large amount must be ingested in order to acquire the necessary supply. Balance studies have shown that with suitable amounts of vitamin D, the child may maintain a desirably positive calcium balance with 24 ounces of milk a day; the larger amount lessens the hazard of inadequate mineralization of bone.[27]

CONSUMPTION OF EGGS

In comparison with the recommended level of consumption, the observed use of eggs parallels in its inadequacy that of milk, with outstanding variations above and below the general average in different regions and during different seasons of the year. The summary of average per capita consumption of eggs from the League's report is set at 199 per annum, or 0.55 egg per day. In some of the midwest states the average level of consumption is considerably greater than this number; the average value reported from certain districts of Kansas was 9 eggs per week;[28] Montana, 10 eggs per week;[29] in Nebraska, during a period of low market value for eggs, the average consumption approximated two a day per capita.[30] In Wisconsin, on the other hand, a report of egg consumption during the winter months indicated that with high market value, very few were used.[31] In a Kentucky survey the consumption averaged an egg per family per day; eggs were almost entirely absent from the winter diet, whereas at the time of greatest yield, only 62 per cent of the children received eggs as often as twice a week. It was stated that eggs were considered as money and that in their stead less marketable products were used.[18] Other reported averages of weekly per capita use were 5.5 in Florida;[32] 4.5 in Georgia;[33] 6.3 in Illinois as a whole, but 8 when the rural consumption alone was considered;[34] 4.6 in Louisiana;[35] 5.5 in Missis-

sippi;[36] 5 in New Hampshire;[24] 8 in rural Ohio;[37] 4 in South Carolina;[38] 3 to 4 in the South Appalachian region;[18] 6 in Utah.[39] It will be recognized that these studies must be corrected for regional and seasonal peculiarities and that much individual variation in consumption exists. In the Gary study, which was cited in the survey of milk consumption, it was found that 60 per cent of the children had eaten no eggs on the day preceding the questioning.[17] In the southern districts eggs were used in fewer numbers by the negro population than by the remainder.

CONSUMPTION OF MEAT

The average annual consumption of beef, pork, and mutton in the United States during the years 1930-34, according to data presented by the League of Nations Committee, totalled 136.5 pounds per capita.[24] The largest part of this, 78.1 pounds, was pork, which because of its high fat content cannot be considered as equivalent in its protein value to the other meats. While much of the fat may be removed and used as lard, large amounts of it are consumed in the form of bacon and salt fat meat. The protein content of pork side meat is only half that of equivalent weights of beef. Correcting the above values for the relative protein content, one may estimate that the average per capita protein ingestion as meat amounts to 27.4 grams per capita per day. This is supplemented by the consumption of poultry and of fish, which is not large considering the country as a whole, but which is quite large in some areas. When used, however, it usually replaces, rather than supplements, the use of other protein foods. In rural Illinois, the annual per capita consumption of chickens is quoted as 10;[34] in rural Kansas, 15.[28] In the states adjacent to the Great Lakes much fish is used; the amount is not stated.[40] In a Florida survey consumption of fish averaged 9 pounds a year per capita for whites, 12 pounds for negroes.

Marked regional differences are noted in habits of meat consumption. Consumption of beef is greater in urban than in rural areas; in the latter the use of pork predominates, especially in the South. In a regional Kentucky survey it is stated that 60 per cent of the rural families have no meat other than fat salt pork for eight months of the year; this however is served three times a day to children and adults alike.[18] Aside from its fat and its low content of protein, this form of meat is of questionable nutritional value. A similar condition prevails throughout the greater part of the South. In general, consumption of meat in these states is too low; yet a disproportionate amount of the food budget as a whole is said to be diverted to this expensive form of food.

Although in parts of the country the protein consumption of the adult members of the population probably exceeds their need, it is doubtful whether many cildhren of any region receive much more than enough to meet their requirements. In the southern states it is very questionable whether a considerable proportion of the population at any age receive protein in sufficient amounts. This is dependent on the low consumption by these individuals of milk, eggs, and lean meat. The high level of consumption of cereals and of legumes probably lessens this deficiency in considerable degree, but in view of the fact that protein from vegetable sources is less valuable to the

human organism than that from milk or meat products, the safety of such a regimen is still open to question. Moreover, dependence on cereal sources for protein usually results in a reduced intake of calcium, vitamins, and iron. From dietary studies alone, one would predict the prevalence of nutritional anemia and hypoproteinemia among many of the inhabitants of the southern states.

CONSUMPTION OF FRUITS AND VEGETABLES

Data expressing the total consumption of fruits and vegetables in rural areas are inadequate, due to lack of accurate information concerning the amount of these foods produced and consumed at home. Yet by observing the number of families raising gardens, the nature and amount of material typically produced, the type and amounts of foods canned, stored or otherwise preserved for winter use, and the extent to which such families purchase these types of foods, an estimate can be made concerning the adequacy of their ingestion. Field surveys indicate quite unanimously the high percentage of farmers who make little or no use of the garden for the production of fresh foods during the growing season, and canning and storage are not utilized in an effective manner. In a Kentucky study[18] it was reported that whereas most families had gardens, only few varieties of foods were raised. Green beans were the vegetable most commonly raised, and the planting of carrots and green vegetables was small in amount. Very few foods were stored for winter. Canning, chiefly of tomatoes, was inadequate in amount. Only half of the families studied stored even potatoes for winter use; in their stead, dried beans were used daily. Although the region was adapted to the production of fruit, 80 per cent of the families raised none, whereas others had only a few peaches or apples. Wild blackberries were used extensively and comprised the only fruit canned by two-thirds of the families. The situation in New Hampshire was quite similar. Although most families had gardens, few used them effectively. Vegetables and fruits were used in season, but home canning averaged only 20 quarts per family. Seventy per cent of the families have trees which bear fruit, yet only half of the people serve fruit twice daily.[24] In the southern states where all-year gardening is possible, the winter garden usually consists only of a patch of turnip greens or of collards. Practically without exception, reports from rural areas throughout the country indicate that although the consumption of fresh foods may approach adequacy during the growing season, their use is very limited at other times, that provision for storage and canning is not adequate, and that but few fresh products are used during the seasons when they must be purchased. Where it is possible to estimate the average annual consumption in terms of their proportion to the total diet, they represent possibly half the amount that has been recommended. In some areas the diet is devoid of vegetables other than dried beans and consists throughout the winter of beans, bread, fat salt pork, and syrup.

CONSUMPTION OF CEREAL PRODUCTS AND OF SUGAR

Cereal foods usually are palatable, cheap, and satisfying as far as the appetite is concerned. It is natural that they should fill a large place in the diet. If restricted to a proper proportion of the total,

their use is to be encouraged. However, when together with fats they usurp a major place in the diet, their use contributes to malnutrition. Moreover, they usually are used in a form which preserves little of their vitamin and mineral content. At best, they contribute nothing unique in nutritional value; as often used, they supply only a form of cheap energy. The use of cereals in a condition approximating their native state would greatly increase their nutritional contribution; this is not practicable because in such form they often are less palatable, are less adaptable in the preparation of baked goods, and become rancid or infested very readily. Limited amounts can be eaten as cooked cereals; many of these as marketed offer little other than starch and vegetable protein. If eaten with milk or cream, the latter has the more outstanding nutritive worth.

Sugar has little to commend it as a food, other than its cheapness, ready availability, ready combination with other foods, energy value, and pleasant flavor. Yet this food comprises the source of a fifth to a sixth of the calories in the average American diet. The data quoted by the League's Committee[2d] indicate an average daily per capita consumption of 4.5 ounces, equivalent to 540 calories. In a New York rural survey, the consumption by younger children was estimated at 3 ounces a day; for men, 5 ounces.[41] The average daily per capita consumption of wheat in 1932-35 is quoted at 0.61 pound, or over 1,000 calories.[2d] In Table I the percentage distribution of calories is expressed in terms of the diet recommended for the child of ten to twelve years by Mrs. Rose,[6] that observed in 224 typical American families as quoted by Sherman,[8] and the results of a federal survey of diets of families of wage-earners and clerical workers in North Atlantic states.[42]

TABLE I

NATURE OF FOOD	PERCENTAGE DISTRIBUTION OF CALORIES		
	PRESCRIBED	OBSERVED	
Cereal products	20-25	38.2	30.25
Fats	13-14	10.32	17.14
Sugar and sweets	6- 8	10.06	12.37
Eggs, meat, cheese, etc.	7- 8	20.76	14.60
Milk and its products	34-38	8.08	9.79
Vegetables and fruits	17-18	12.04	14.74

The values expressed in the two general diet averages represent foods served to both children and adults, whereas the prescribed foods are designed specifically to meet the needs of the child. The latter will be somewhat higher in milk products than is essential for the adults, although the same regimen may be used for each with profit. The preponderant use of meat products in the observed dietaries compensates in an inadequate manner for the deficiency of milk, in a form which is economically extravagant. The preponderant use of cereals and sweets and lessened consumption of vegetables in the observed dietaries is noteworthy. Data regarding sugar consumption indicate that more is consumed than meal surveys reveal. Possibly this is due to the consumption of candy and other sweetened products apart from the meals. Otherwise it suggests an inordinate use of sugar by some individuals as compared with the average data for the whole group.

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ECONOMIC FACTORS IN THE NATURE OF THE DIET

Within the lower brackets of income, there is direct relationship between the expenditure for food and the quality of the diet. In a comparison of purchases by families whose weekly food expenditure ranged from $1.20 to $4.17, the use of each type of foodstuff increased with the amount expended for the diet as a whole; the most marked increase was in vegetables and fruits, and next in meat products. Of these, fresh foods showed gains out of proportion to dried products, yet the use of canned fruits increased markedly. Other aspects of the same study, which was conducted in typical areas of the North Atlantic, Pacific and east South Central industrial districts revealed that individual diets may fail to correspond in adequacy to the level of expenditure.[16] It was found that in each region some families managed to maintain quite satisfactory dietaries even with minimal outlay, whereas similar numbers failed to receive satisfactory foods even at the upper level of expenditures. With the negro families it has been noted that with increased outlay, the tendency is to buy larger amounts of the same poorer quality foods used by those in the lower brackets. In each industrial region studied, the average food consumption was very inadequate with minimal expenditure, and did not become dependably satisfactory except in the higher brackets. A weekly expenditure of $2.00 or more per capita appeared necessary as a minimal average allowance for adequacy.

In the rural studies reviewed, it may be observed almost without exception that food consumption is determined in large measure by the nature and amount of produce raised at home. In most areas local production for home use falls far behind its possibilities, and measures for the preservation of food are generally inadequate. Where products have a good market value, they are more often sold than used. In the single-crop regions, especially those farmed by small renters, there is resistance to the use of lands for garden purposes. During the time when such crops had low market value, the use of the land for small gardens increased, but with restoration of good prices the practice was discontinued.

Another obstacle to the improvement of the level of diets is the ignorance and indifference which is commonly encountered in regard to the body's food needs. The people have become so accustomed to eating as a source of pleasure or as a means of silencing hunger that they do not recognize nutritional requirement beyond these ends. Campaigns of education through demonstration units, school programs and extension work in farmers' organizations probably will prove the most effective agencies. While elevation of the standard of living in the underprivileged groups will relieve some of the more glaring nutritional defects, the habits of whole communities will have to be altered before good conditions will prevail in them.

In a considerable proportion of the children of these who are financially able to afford good food, the intake falls below the requirements for optimum health. This must be attributed to unfamiliarity with the importance of proper eating. In the terms of elements of nutrition, these deficiencies concern chiefly the intake of calcium, protein, vitamin D, and in lesser measure vitamins A, C, and G. In terms of

foods, these deficiencies reflect inadequate use of milk, fruits and vegetables, and deficiency of vitamin D either as sunshine or as one of its food sources such as cod liver oil.

In a recent discussion of dietary inadequacies in the British Isles, a correspondent quotes Mellanby on the delay in general utilization of the nutritional discoveries of the past two decades.[43] If the problem had been one which applied primarily to adults rather than to the oncoming generation, it would have received more acclaim. To expect healthy, strong adults, it is necessary to feed them well during the period of growth, not merely to prevent disease, but to build for the best possible health. The comment continues by stating that the superior athletic ability of the Finns as compared with the British youth is less mysterious when it is remembered that the daily milk consumption of the former is three times as great as that of the latter.

SUMMARY

Statistics concerning average food consumption and surveys of eating habits establish that the American diet is decidedly below the standard of optimum adequacy. Even among those who can afford the best, many individuals receive poor diets. In the poorer groups, the incidence of poor nutritional habits is vast. Such a situation inevitably lowers the level of health of the population. Certain measures would aid in the correction of these conditions. Educational measures should be directed toward familiarity with relative food values. This should lead to the increased use of milk and its products, vegetables, and fruits. In rural areas the encouragement of home production of valuable foods and their preservation for use throughout the year would be most important. In urban areas it is necessary to familiarize members of households with proper distribution of expenditure for food so that less may be spent for foods of low biologic worth, and more for those which are more essential. In many areas, the readjustment of food habits would be relatively minor, whereas in others it will be necessary to bring about marked reorganization of the dietary regimen if outstanding malnutrition is to be corrected.

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40. Stencil Bulletin, Feb., 1937; Agricultural Experiment Station, Madison, Wis.
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42. Monthly Labor Review (July, 1936) Bureau of Labor Statistics, U. S. Dept. of Labor, Washington, D. C.
43. Foreign Letters, J. A. M. A. **109**: 2149, 1937.

American Academy of Pediatrics

Proceedings

SEVENTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

JUNE 2-4, 1937

WALDORF ASTORIA HOTEL, NEW YORK

Round Table Discussion on Diabetes

Chairman: Elliot P. Joslin, M.D., Boston, Mass.
Assistant: Priscilla White, M.D., Boston, Mass.

CHAIRMAN ELLIOT P. JOSLIN.—Before proceeding with the round table discussion, I would like to say a few words about the incidence of diabetes in children. I believe that there are about twelve thousand diabetic children under the age of twenty years and eight thousand under the age of fifteen years in this country now, whereas before insulin, the frequency was one thousand cases per year. Dr. White feels there is one diabetic child for every eight thousand normal children. The exact incidence is not definite. Reliable statistics indicate that there are probably between ten thousand and eleven thousand diabetic children living in the United States. The number of unclassified cases is going way up.

The mortality before insulin was discovered was quite high. One thousand children afflicted with diabetes died per year in the United States in the preinsulin days. The discovery and use of insulin has changed this gruesome picture greatly. Now one child in one hundred dies per year. The present-day diabetic child will outlive the doctor.

Years ago it was difficult to settle the question whether or not a child was a diabetic. The repeated venipuncture resorted to years ago was an obstacle to diagnosis. Today a capillary blood sugar test for diagnosis is a relatively simple procedure and has replaced the venous blood sugar determination.

An interesting question is how many patients with glycosuria later turn into true diabetics. This question has received special study by Dr. Marble at Colorado Springs, will be reported upon, and will appear in the near future in the *Journal of Medical Sciences*. Patients with renal glycosuria should be watched during life.

A blood sugar determination in children having upper respiratory infections is unreliable. It should therefore be remembered that a blood sugar determination for diagnosis does not count in the presence of an infection, i.e., "cold in the head."

A word should be said about the duration of life of juvenile diabetics. Here again the picture has changed. No diabetic patient under nineteen years of age died in Boston in 1935. In Stettin there was no death in coma during one recent year. I quote from a recent study by the Metropolitan Life Insurance Company. A child afflicted with diabetes at the age of ten years and treated has a life expectancy of 31.7 years. Now compare the life expectancy of a diabetic individual at the age of sixty-five years with that of a normal person at the same age. The life expectancy of a diabetic at the age of sixty-five years is eight years, that of an apparently so

called normal good health non-diabetic person at the same age is twelve years. In other words, the average diabetic child today has a better chance of living longer than the average doctor, for it has been repeatedly demonstrated that the average practitioner enjoys his art of medicine for a period of approximately thirty years.

Now, what are the causes of death from diabetes in children? (1) Diabetic coma, (2) pulmonary tuberculosis, (3) infections, (4) hypoglycemia, (5) accidents, (6) miscellaneous causes.

Table I gives the incidence of death from these causes since introduction of insulin in 1922.

TABLE I

RESULTS OF FIFTEEN YEARS' TREATMENT OF 1,063 DIABETIC CHILDREN—AUGUST, 1922-1937

	LIVING 959		DEAD 104									
DATE	DEATHS COMA		DEATHS—NONCOMA									
			TUBERCULOSIS		INFECTIONS		HYPOGLYCEMIA		ACCIDENTS		MISCELLANEOUS	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
1922-1927 Total 35 Av. duration 2.7 yr.	32	91	0	0	3	9	0	0	0	0	0	0
1927-1932 Total 27 Av. duration 4.7 yr.	11	70	2	8	3	11	2	8	1	4	0	0
1932-1937 Total 42 Av. duration 9 yr.	18	43	7	15	11	25	2	5	1	2	3	7

Diabetic coma is the most important single contributing cause of death in the diabetic child. It is absolutely needless. For the past fifteen years the incidence of children dying of diabetic coma is high. Even with the use of insulin today, more children are dying with diabetic coma than before the time when insulin was discovered. As an illustration, I know of a child who was admitted to one of our modern hospitals in a state of coma. Six hours elapsed before a diagnosis was made. Death occurred.

What happens to children who do not die of diabetic coma? By referring to the chart you will find that in our study during the first five-year insulin period the average duration of life was 2.7 years and that there were no deaths from tuberculosis, during the second five-year insulin period the average duration of life was 4.7 years with only two deaths, or 8 per cent, and during the last five-year period with insulin seven deaths were due to tuberculosis, or 15 per cent. Thus *in toto* of nine children who had diabetes and died of tuberculosis, the shortest duration of life was five years and the longest fifteen years.

DR. ALFRED FISCHER (NEW YORK CITY).—Do you do a routine tuberculin test in addition to x-ray of the lungs?

DR. WHITE.—We hope to test each child in camp this summer.

DR. CARL FISCHER (PHILADELPHIA).—Is there a greater tendency for the child to develop adult tuberculosis if he has had a primary tuberculosis?

CHAIRMAN JOSLIN.—I think so because all our patients have had calcified areas showing earlier infection.

DR. J. C. MONTGOMERY (DETROIT).—What is the incidence of positive tuberculin reactions in diabetic children?

Page 257, line 11:

"One in five shows, by x-ray, evidence of old or recent pulmonary tuberculosis."

Corrections in "Round Table Discussion on Diabetes," February, 1938, Issue

Dr. Elliott P. Joslin requests readers to paste these corrections on the proper pages in the February issue of the Journal:

Page 256, line 3 below table:

"Even with the use of insulin today a greater percentage of children are dying with diabetic coma than was the case for all diabetics (adults and children) before the time when insulin was discovered."

DR. WHITE.—Forty per cent of diabetic children in Boston have positive tuberculin tests and 65 per cent tracheobronchial adenitis with calcification.

DR. MONTGOMERY.—Is there any explanation for the terribly high incidence of tuberculosis seen in diabetic children?

CHAIRMAN JOSLIN.—No, except this one point. Many of the children have been "contacts" with adults who had open lesions.

DR. WM. A. SCHONFELD (NEW YORK CITY).—I would like to ask if the incidence of diabetes is greater among tuberculous patients?

CHAIRMAN JOSLIN.—No, the incidence of diabetes among tuberculous patients is not great, although the diabetic child is ten times more likely to develop tuberculosis. One in five has pulmonary tuberculosis.

In a certain Massachusetts sanatorium, however, statistics indicate that this incidence has risen within the past few years from one in one hundred cases to one in thirty.

DR. SCHONFELD.—What is the outlook of a diabetic patient who acquires tuberculosis?

CHAIRMAN JOSLIN.—Diabetics do very well in sanatoriums.

DR. SCHONFELD.—Does the management of tuberculous patients afflicted with diabetes differ materially from that of nondiabetic tuberculous individuals?

CHAIRMAN JOSLIN.—No, the management is essentially the same as with nondiabetic tuberculous patients.

DR. JOHN M. HIGGINS (SAYRE, PA.).—Is the incidence of tuberculosis in diabetic children on the increase?

CHAIRMAN JOSLIN.—The death rate has been going up; the incidence of new cases has been going down.

DR. HIGGINS.—Is there reason to believe that, with appropriate management of the case, the incidence of tuberculosis death rate in diabetic children will be still less?

DR. WHITE.—Yes.

CHAIRMAN JOSLIN.—**"A curious observation is that after three years following coma one diabetic out of every eight develops tuberculosis."**

Of infections, 9 per cent occurred during the first five-year period, 11 per cent during the second, and 25 per cent during the third five-year period.

DR. ALFRED FISCHER.—In regard to infections in diabetic children, such as acute appendicitis, which, by my experience, is way over the average, is there any theoretical explanation? Does diabetic tissue show less resistance to infections?

CHAIRMAN JOSLIN.—We have had many cases. Appendicitis is often fulminating. (He cited example of patient dying from diabetic coma after being operated for appendicitis.) Pain, nausea, and vomiting are frequent symptoms of diabetic coma. The appendicitis problem works both ways. Now a reaction from protamine insulin complicates the clinical picture because of nausea and vomiting. Rule is: operate if in doubt.

Four children in all died from hypoglycemia, one child died in one of our best hospitals before the result of the micro-blood sugar determination came in. Another child received two hundred units of insulin; Dr. White loaded this patient down with carbohydrates, but she did not survive. Will Dr. White tell about the suspected hypoglycemia death yesterday?

DR. WHITE.—The girl referred to had had diabetes for seventeen years. An appendectomy was performed, and on the fourteenth day she was ready for dis-

charge. She had given herself fifteen units of insulin at 11:40 A.M. She appeared so ill following the injection of insulin that the nurse thought that she had hypoglycemia. Thereupon one pint of orange juice was administered to the patient. The patient died after complaining of pain in the chest. The clinical diagnosis was pulmonary embolism, which was confirmed at autopsy. At autopsy there was a fatty liver. The pancreas weighed less than 60 grams.

CHAIRMAN JOSLIN.—Here is an instance which would have been incorrectly labelled and diagnosed death due to insulin shock if an autopsy had not been performed. Many cases of supposed death from insulin shock have proved to be due to pulmonary embolism. Therefore, when you have patients who are said to have died of insulin shock, think twice. According to Dr. Hartmann, hypoglycemia occurs also in nondiabetic children.

In our series of patients there were only two deaths due to accidents. Among the miscellaneous causes, two deaths were due to pregnancy (one eclampsia and the other following an abortion). One death was due to cerebral hemorrhage. Interesting in this connection are the observations of Bourchadart, who in 1875 said that he had not seen a single pregnancy among diabetic women. In 1905 Naunyn stated that he had seen one pregnant woman who had diabetes. Dr. White has studied the records of three hundred pregnancies among two hundred diabetic women. Now it is quite a luxury to have a diabetic pregnancy. It costs a lot to have a diabetic pregnancy, as Dr. White will tell you.

DR HIGGINS.—Will you sketch the care of the newborn infant whose mother is a diabetic?

DR. WHITE.—A premature infant born of a diabetic mother does not breathe well. Upon birth the infant is placed in an oxygen helium chamber, which consists of a mixture of 25 per cent oxygen and 75 per cent helium. Such a procedure, at present, must necessarily be limited for hospital routine.

The chief danger to these infants is from asphyxia. In addition to the oxygen chamber, referred to, we aspirate them. Many of these babies have fluid in bronchi. An attempt is made to stimulate the respiratory center and improve circulation. Alpha-lobelin and coramine are frequently employed.

Water by mouth is not given during the first twenty-four hours. Mouth feeding is also avoided during the first twenty-four hours. After that period, routine feeding is followed. Babies of diabetic mothers are usually hypoglycemic.

A blood sugar estimation is made at birth and every three hours. If the blood sugar remains above 50 mg. per 100 c.c., we do not worry about hypoglycemia. A blood sugar above 50 mg. is normal. On the other hand, if the blood sugar drops below 50 mg., glucose is administered parenterally, not by mouth. Fifty cubic centimeters of a 5 per cent glucose given intramuscularly, bilaterally, is of value.

DR. HIGGINS.—Is your rule invariable? Do you permit breast feeding?

DR. WHITE.—The procedure outlined is that form ordinarily followed. We are primarily concerned about the welfare of the mother. Lactation is often defective in diabetics. Then, too, many of the infants have been delivered by cesarean section.

CHAIRMAN JOSLIN.—We have a pediatrician and expert premature nurses present at the births of children of diabetic mothers.

DR. HIGGINS.—After the first twenty-four hours, do you proceed along the orthodox method?

DR. WHITE.—Yes.

DR. HIGGINS.—Approximately, how many of the offspring of diabetic mothers fall below 50 mg. in blood glucose?

DR. WHITE.—About 20 per cent.

DR. HIGGINS.—What is the prognosis for such infants?

DR. WHITE.—If they survive the first twenty-four hours, they usually progress favorably. However, such infants should be constantly watched.

DR. HENRY F. HELMHOLZ (ROCHESTER, MINN.).—Why do you not give glucose routinely?

DR. WHITE.—The procedure is undoubtedly wise, but we are studying the blood sugar curve of these infants.

DR. HELMHOLZ.—What strength parenteral sugar do you administer by clysis?

DR. WHITE.—Five per cent glucose.

DR. HELMHOLZ.—Any irritation?

DR. WHITE.—No. In his paper the day before yesterday, Dr. Hartmann advocated three minims of adrenalin (1:1000) to forestall hypoglycemia.

DR. MONTGOMERY.—Can you tell us approximately how many of your babies have required glucose parenterally?

DR. WHITE.—About 20 per cent.

DR. FRED W. BUSH (ROCHESTER, N. Y.).—What is the percentage of hypoglycemia in newborn? We have one newborn with blood sugar of 49 mg. per cent.

DR. WHITE.—The data for newborn children are insufficient in number. We had one baby with 9 mg. per cent blood sugar.

CHAIRMAN JOSLIN.—Hypoglycemia may occur in the newborn of diabetic mothers. It is by no means universal. Be careful not to kill with treatment. Be careful about giving fluids by mouth (asphyxia?). Glucose might best be administered rectally or subcutaneously. Dr. West in Dr. Bertnard Smith's Clinic in Los Angeles is studying this subject.

DR. EARL F. KELLY (PAWTUCKET, R. I.).—What is your educational program? Do you educate the mother, child, or both?

CHAIRMAN JOSLIN.—Both. A two-year-old child comes in with diabetes. The responsibility often falls on the child at ten years, especially if the mother does not have control of the child.

DR. ALLEN.—What do you do with the adolescent rebelling against regime?

CHAIRMAN JOSLIN.—This is a common behavior reaction, especially among girls. (1) Association with others. Most striking example was a fourteen or fifteen-year-old girl, mentally disturbed, with colitis and abdominal pain. Treatment: large private school away from home where there were three other diabetic girls. (2) Obese child found herself by helping her father in business. (3) Summer camps. (4) Boarding school. (5) Explain that the disease is not necessarily progressive. (6) Example of successful careers of others.

DR. ALVAH L. NEWCOMB (CHICAGO).—Do you need pyschiatric help often?

CHAIRMAN JOSLIN.—Yes.

DR. ALLEN.—What do you do with the poor boy who is rebelling?

CHAIRMAN JOSLIN.—One learned radio. Another has behaved nicely at Prendergast Preventorium, which is a sort of boarding school.

DR. WALTER LEVY (NEW YORK CITY).—What is the frequency of lipemia in general with diabetes? (He cited a case with blood cholesterol and blood fat of 900 mg. which responded readily to regular insulin.) What are the subsequent connections to arteriosclerosis?

CHAIRMAN JOSLIN.—These questions cover a tremendous field. Our last patient with lipemia with diffuse xanthomatosis died in New York City without an autopsy. Lipemia retinalis has been observed in 1 in 1000 diabetics. Hypercholesterolemia is rare today in any patient taking carbohydrate, 150, and a moderate quantity of protein and fat.

DR. HIGGINS.—I would like to ask a question that is not exactly a pediatric problem. Do you make an effort to discourage diabetics from marrying?

DR. WHITE.—I do not think we have ever done so, although diabetes is a hereditary disease. We might, however, discourage child-bearing.

CHAIRMAN JOSLIN.—It is not so bad when one diabetic marries another who is nondiabetic, but we are absolute in saying that two diabetics must not marry and have children.

DR. HELMHOLZ.—Have you known of any such cases, in which two diabetics married, and the result of such pregnancies?

DR. WHITE.—Yes. Twenty-four per cent of the offspring developed diabetes.

CHAIRMAN JOSLIN.—Dr. White can give you some interesting figures relative to this incidence.

DR. WHITE.—The following figures are self-explanatory.

	CORRECTED EXPECTATION	IDENTIFIED
Cross between two diabetics	100%	24%
Cross between diabetics and carriers	40%	10%
Cross between carriers	16%	4%

DR. J. B. STONE (RICHMOND, VA.).—Is there any difference in the incidence of complications among the newborn diabetics and newborn infants of nondiabetic mothers?

DR. WHITE.—Of the newborn of diabetic mothers 60 per cent developed asphyxia. Congenital defects have been reported in the literature. Also there is the problem of hypoglycemia, as has already been referred to.

DR. E. ALBAGER (CINCINNATI, OHIO).—How many days must elapse before you can consider the newborn infant out of danger?

DR. WHITE.—After the first twenty-four hours.

DR. M. HINES ROBERTS (ATLANTA, GA.).—What is the association of asthma and diabetes?

DRS. JOSLIN AND WHITE.—About one per cent. Have you had any cases?

DR. ROBERTS.—Two recently.

DR. WHITE.—Dr. Kerr says the association is very infrequent. The whole problem was discussed at the American Association of Physicians about three years ago.

DR. H. CHANDLER CLARKE (NEW ROCHELLE, N. Y.).—What is the relationship of allergy to diabetes? I have under my care a child who, every time he cries, gets a neurodermatitis. His blood fasting sugar is 98 mg. per 100 c.c.

DR. WHITE.—It is an established fact that allergy runs in families of diabetics, tending to skip the patient.

DR. CLARKE.—Are such patients good risks for tonsillectomy?

DR. WHITE.—We have never had any trouble with them.

Protamine Insulin

DR. WHITE.—The mortality rates of the preinsulin era long ago answered in the affirmative the question, "Should insulin be used in the treatment of juvenile diabetes?" But wonderful though insulin was, the fundamental characteristics of juvenile diabetes, severity, instability, and progression, led to a certain amount of dissatisfaction. The severity and progression are indicated by the tendency toward elevation of the fasting blood sugar in successive years of duration until the fifth year, when stabilization has generally occurred. To counteract this, students of diabetes in the past have administered large doses of insulin late at night or in the early morning. Though effective, too often they were omitted by parents and children who feared night hypoglycemia. The child, whose fasting blood sugar is three or four times the normal, awakens with exhaustion and nausea, and is unable for many hours to carry on the normal activities of a child. This was the state of affairs until 1933 when Dr. Hagedorn formulated his new working hypothesis, discovered protamine insulin, and for clinical trial administered it to patients with severe juvenile diabetes who, treated with the old technique, had a characteristic W-shaped blood sugar curve. When he administered a dose of regular insulin in the morning and protamine insulin at night, he flattened the curve to that of a normal or mildly diabetic individual.

The work with protamine insulin advanced rapidly, for Dr. Best demonstrated the physiology of the single time technique already advocated by Wilder and Campbell, namely, that the size of the dose of protamine up to a certain point controlled the duration of action in the body. In the Connaught Laboratories zinc was added to protamine, doubling the efficiency of the preparation.

The technique of desugarizing a new patient with protamine insulin is not difficult, and the size of the dose is based upon the age of the patient.

YEARS	DOSE (UNITS)
0- 5	10
5-10	20
10-15	20-30

This may be increased gradually to forty or fifty units, but, if this limit is reached, accessory doses of regular insulin are indicated.

With long-standing cases the replacement is more difficult. Though it is not a hard and fast rule, we generally begin with two units of protamine to one of regular insulin. When the fasting blood sugar drops, the need for regular insulin decreases.

From September, 1935, to June, 1937, some four hundred children have been adjusted to protamine insulin, 97 per cent with the single time technique, only 10 per cent with protamine insulin alone. The age, the duration, and consequently the severity of diabetes have controlled the size of the dose of insulin.

The need for regular insulin is indicated by the level of the blood sugar at 11:30 A.M. The two doses of insulin are administered separately but at the same time.

The carbohydrate content of the diet is not quite so liberal with protamine insulin as with regular insulin. Most of the time we employ 2 (C.): 0.9 (P.): 1(F.) ratios. The total calories have been based upon basal metabolic studies; the rates of growth, upon periods of prolonged observation at camps and boarding schools, and the appetite of the child.

AGE YEARS	CALORIES
1	1000
5	1400
6-10	1600-1800
11-15	1800-2000
16-20	1800-2500

The great advantage of protamine insulin is, we believe, not only the greater comfort of the single time technique, but the number of hours of controlled diabetes, which should have a profound effect upon the prevention of degenerative complications in the future.

DR. L. HAYS (TULSA, OKLA.).—If population is considered in general for diabetic as well as nondiabetic individuals, have you any idea how in many cases such urines would be sugar positive?

DR. WHITE.—I have no idea. I do not think such work has ever been carried out.

DR. CLARKE.—Frequently I receive word from the laboratory when a request for a tolerance test is posted, asking me if I want a two-hour tolerance test. Will you explain what is meant by a two-hour tolerance test and which form of tolerance test you prefer?

CHAIRMAN JOSLIN.—For the glucose tolerance test, 1 gram of glucose is given to the patient per pound of body weight. A blood sugar estimation is made in one hour and again in two hours. If the blood sugar is 200 mg. per cent with sugar present in the urine, that individual is diabetic. If the blood sugar is 170 mg. per 100 c.c. of blood, or below this figure, he is not diabetic. You can use both the capillary and venous methods. A diagnosis of diabetes is reached by the peak of the blood sugar curve and by the presence of sugar in the urine. A capillary blood sugar level of 200 mg. per 100 c.c. or above, or a venous blood test of 170 mg. per 100 c.c. or above is quite diagnostic. Never diagnose a person as a diabetic on a single tolerance test. Wait a little while, and do another.

DR. CLARKE.—How often are readings taken?

DR. WHITE.—One-half hour, one hour, and at two-hour intervals.

CHAIRMAN JOSLIN.—Never make a diagnosis of diabetes unless sugar is present in the urine.

DR. ROBERT A. KNOX (WASHINGTON, PA.).—What are the important complications seen in diabetic children?

DR. WHITE.—There are seven important complications met with in diabetic children:

1. Coma.
2. Loss of resistance to infections, local and general.
3. Premature development and degenerative changes.
4. Deficiency disease.
5. Metabolic disturbances of the skin.
6. Dwarfism.
7. Hepatomegaly.

Of these complications we shall discuss two, dwarfism and hepatomegaly.

Failure of growth and development has occurred in 5 per cent of our diabetics. We define as dwarfism or pseudodwarfism those cases in which the height deviates from 4 to 13 inches below the standard for age. The condition has followed rather than preceded diabetes. Besides the failure of growth these children have delayed dentition, silky hair, lanugo hair, delicate skin. The intelligence is generally normal. The condition appears to be a physiologic contradiction, for it is overactivity rather than underactivity of the pituitary that we associate with diabetes. Whether dwarfism is the result of diabetes or its treatment or whether they are coincident conditions remains a problem for future solution.

Male predominance was the rule.

The children have been treated with high caloric, high protein diets, later with the addition of thyroid, and still later the addition of growth hormone; we believe we

Page 262, line 17:

"If the blood sugar is 130 milligrams per cent fasting (venous or capillary) or below this figure, he is not diabetic."

have obtained good results with hormone therapy. The rates of growth doubled after its administration. However, these children were also treated with protamine insulin, and we believe the acceleration of growth is greater with protamine than with regular insulin. The physiology for this has been demonstrated by Dr. Wilder, who has shown the greater retention of nitrogen with protamine than with regular insulin.

Enlargement of the liver has been observed in 5 per cent of our diabetic children. The size of the liver is not insignificant. The edge can be traced in the lower abdomen and x-ray reveals it often in the pelvis. Many of the children are dwarfish. They have large, protuberant abdomens with dilated veins. The kidney, the spleen, and the heart may also be enlarged.

Many have had severe attacks of abdominal pain.

The nature of the enlargement is not clear. It may be due to glycogen or fat or both. None has come to biopsy or autopsy. Chemical tests reveal little. A rise of blood sugar occurs after the administration of adrenalin and the blood fat studies are essentially normal. Liver function tests have revealed no abnormality. The lipolitic ferments were diminished.

The lesions have been produced experimentally by Best, by the omission of choline in the diet and the administration of anterior pituitary substance. We have treated such cases with betaine hydrochloride, a cholinelike substance, and also by protamine insulin; the better results were obtained by protamine insulin. This was reported by Hanssen of Hagedorn's clinic.

DR. KNOX.—Upon what criterion do you base your standard of undergrowth?

DR. WHITE.—Upon standard height scales. If a child's height is more than 4 inches below the standard—this is considered abnormal.

DR. KNOX.—What is the percentage of retarded growth in diabetic children?

DR. WHITE.—Five per cent of diabetic children fail to grow normally.

CHAIRMAN JOSLIN.—Has anyone tried antuitrin-G?

DR ALFRED FISCHER.—No results. Also bad reactions to thyroid medication.

CHAIRMAN JOSLIN.—When epiphyses have closed, cases are pathetic.

DR. WHITE.—One child grew at nineteen and twenty years.

DR. JOHN A. MONTFORT (BROOKLYN, N. Y.).—I have used it with excellent results. One child gained 1¾ inches in eight months.

DR. KNOX.—What is the dosage, and how do you gauge the anterior pituitary hormone?

DR. WHITE.—Three cubic centimeters are administered every other day only to patients whose epiphyses are open.

DR. LEROY STOKES (HAVERHILL, MASS.).—What is the incidence of enlarged livers in diabetic children?

DR. WHITE.—Five per cent of the patients have enlarged livers.

DR. CLARKE.—Do you also find enlarged livers in younger diabetic children? Does the enlargement of the liver bear any relationship to the deposition of subcutaneous fat, skeletal growth—dwarfism?

DR. WHITE.—Yes, it seems that everything in the growth and developmental system is retarded, the bones, development of the teeth, etc.

DR. CLARKE.—Does the use of protamine insulin improve such conditions?

DR. WHITE.—Yes.

DR. NEWCOMB.—The children treated with protamine insulin appear more like normal children. They are leaner, with smaller abdomens. Gain in height is accelerated, particularly in pseudodwarfs with large livers.

DR. HAYS.—Is it true that the adjustment of a long-standing case of juvenile diabetes is more difficult by means of protamine insulin?

DR. WHITE.—Yes.

DR. C. V. CALVIN (BRIDGEPORT, CONN.).—Will you discuss the reactions incident to the administration of protamine insulin?

DR. WHITE.—At first it was thought that protamine insulin did not produce severe reactions. We now know that it does. Protamine insulin may produce severe reactions—usually delayed. Nausea, vomiting, and headache are seen in patients who receive protamine insulin. The skin sometimes becomes dry instead of moist. In this respect protamine insulin differs from the reaction of regular insulin. As a matter of fact, the patient will resemble one in coma, and differentiation must be based upon laboratory methods. This reaction is seen from 4 to 6 A. M.

DR. GEORGE W. CALDWELL (NEW YORK CITY).—Have the diets and caloric requirements changed since institution of protamine insulin?

CHAIRMAN JOSLIN.—Not essentially.

DR. J. B. STONE (RICHMOND, VA.).—Do diets have to be changed with the use of protamine insulin?

DR. WHITE.—Before the days of protamine insulin we used two to one, or three to one carbohydrate-fat ratios. With protamine insulin we employ a two to one carbohydrate-fat ratio.

DR. STONE.—What would you say is the great advantage in the use of protamine insulin?

DR. WHITE.—The one-time technique of administration of insulin (before breakfast), the assurance of normal growth and development, and the prevention of complications.

CHAIRMAN JOSLIN.—I would like to say that, from a study of twelve hundred cases of diabetes treated by means of protamine insulin by the Metropolitan Life Insurance Company, the control of diabetes was found to be definitely better with protamine insulin than with insulin. In this survey there was not a single patient treated by protamine insulin who ever went back to insulin. Another advantage in giving protamine insulin is that it reduces the frequency of injections.

DR. J. G. BROWN (SASKATOON, SASK., CANADA).—Do you ever figure out the carbohydrate of the diet and allow the patient to choose the protein and fat?

DR. WHITE.—We have not allowed that schedule (Stolte). It works better with the older patient who actually eats with moderation. How many give less carbohydrate with protamine insulin? (Majority used about the same carbohydrate.)

DR. CLARKE.—Why do some children do badly when the treatment is changed from insulin to protamine insulin?

CHAIRMAN JOSLIN.—With protamine insulin you do not begin to get the blood sugar under control for several days. The change of the blood sugar curve is a slow, not a rapid change. This takes time and patience. Protamine insulin means that you must spread the meals out during the day. Protamine insulin acts "while you sleep." It acts between meals and controls the patient for twenty-four hours. Results are from summation of effect. The use of protamine insulin

Page 264, line 33:

"In this survey there was not a single child patient up to the spring of 1937 treated by protamine insulin who ever went back to regular insulin." (Since that date there have been few such cases.)

does not necessitate living on protein so much. Patients can therefore utilize their carbohydrates better, for, as you know, diabetics do not have much stored carbohydrates. One of the big advantages is simplicity of treatment. Do not change dosage frequently. Be slow in conclusions.

DR. ALPER M. WISE (BROOKLYN, N. Y.).—What do you do with patients who absorb protamine insulin irregularly?

CHAIRMAN JOSLIN.—I just do not know.

DR. MONTGOMERY.—Is protamine insulin preferably given at night instead of the morning?

DR. WHITE.—With adults it has been used but not with the child in our clinic.

DR. NEWCOMB.—What has been your experience with U 80 protamine?

CHAIRMAN JOSLIN.—We have been unable to detect any difference in action and have so informed the manufacturers. We expect reactions from mistakes with the greater concentrations. I know of no fatal cases with protamine insulin, 5 or 6 fatalities with the regular insulin. Of cases of all ages treated with protamine, five hundred were treated with protamine insulin alone, seven hundred fifty treated with protamine and regular insulin.

DR. HAROLD L. VOGEL (JACKSON HEIGHTS, N. Y.).—Can you give both regular and protamine insulin in the same syringe barrel?

CHAIRMAN JOSLIN.—Dr. Butler mixes the two insulins and gets, to some extent, the effect of each. Our results were not very satisfactory. We hope to have eventually a clear instead of a cloudy protamine.

DR. WHITE.—We attempted to layer the two insulins. This is difficult. Some of the regular will be converted to slowly acting insulin. But, if we mix the two insulins and give relatively more of the regular and less of the protamine than previously given, we may get the desired effect.

DR. ROCKWELL M. KEMPTON (SAGINAW, MICH.).—How is one to judge whether to prescribe protamine insulin alone or protamine with a supplementary dose of regular insulin?

CHAIRMAN JOSLIN.—Usually one is able to get a normal morning blood sugar with protamine insulin alone, but loss of control will appear at noon or in the afternoon. Regular insulin is prescribed in the morning to manage the forenoon hyperglycemia and glycosuria. Dr. Himsworth of England had written reporting good results the next day, when protamine was prescribed at 11 P.M. A patient with a carbohydrate of 240 required 40 units of protamine at the onset. Insulin requirement has now dropped to 12 units, but this is a most exceptional case. Protamine protects the child's health.

DR. WISE.—How low a blood sugar have you seen without a reaction?

CHAIRMAN JOSLIN.—Do you mean the lowest blood sugar encountered in diabetic patients without the appearance of symptoms?

DR. WISE.—Yes.

DRS. JOSLIN AND WHITE.—Thirty milligrams per hundred cubic centimeters without symptoms.

DR. WHITE.—Twenty milligrams per hundred cubic centimeters without bad symptoms.

DR. MONTGOMERY.—Will you tell us how you manage the acute diabetic at the onset of an acute infection?

DR. WHITE.—We do one of two things: reduce the diet to C. 150, P. 50, F. 50, and either administer regular insulin every three hours according to the fraction, or continue with protamine insulin and give supplementary doses of regular insulin at noon, 6:00 P.M., and 10:00 P.M.

Regular Insulin Units	15	10	5
Color of Benedict Test	Red or Orange	Yellow	Yellow Green

DR. C. H. WAYMULLER (BROOKLYN, N. Y.).—Do you nearly always have to give intravenous glucose for protamine insulin shock?

DR. WHITE.—No, not as a rule.

DR. WISE.—How much carbohydrate can a diabetic utilize?

CHAIRMAN JOSLIN.—None of us knows. It is a very difficult thing to standardize a diabetic's tolerance.

DR. CLARKE.—I would like to ask two questions for practical purposes:

1. A diabetic youngster is on regular insulin. I desire to change over to protamine insulin. Is it a rule to give two-thirds of the regular dose of insulin?

2. In a growing child, do you give a high protein diet?

CHAIRMAN JOSLIN.—1. All of us who work with diabetics have individual ideas, sixty units of insulin a day, divided into three doses of 20-20-20. I would give 20 units of regular insulin in the morning and then would hedge and give 30 or 36 units of protamine insulin.

Question 2 was answered by Dr. White.—The ratios we use are C.2, P.0.9, F.1.

CHAIRMAN JOSLIN.—I have not seen a single instance of insulin atrophy (subcutaneous fat) with protamine insulin. I have seen such change when ordinary insulin was used.

DR. W. J. SCOTT (DETROIT, MICH.).—I would like to present the case history of two juvenile diabetics and ask your advice about their treatment.

H. B. K., Jr. was born Dec. 9, 1932, and was first seen by us at the age of three months and was followed regularly until the age of two years. He had no acute infections except one mild cold during this period. At the age of two years, he weighed 26 pounds 10 ounces, and was 32 inches tall. We felt that his slight undernutrition was due to excessive activity. He was not seen again until Sept. 25, 1935, a period of nine months, because he had been, to all intents and purposes, well. The mother brought him in to see us because his appetite was unusually good, and he was failing to gain in weight. He also was drinking lots of water. The physical examination at this time was entirely negative except for the above-mentioned undernutrition. Urinary sugar 4-plus. Fasting blood sugar (Sept. 28, 1935) 105 mg. Two days later, the blood sugar was 320 mg. An appropriate diabetic diet was outlined with 5 units of regular insulin twice a day. The weight at this time was 27½ pounds, a gain of only 14 ounces in nine months.

This child has progressed very satisfactorily, his parents having adhered rigidly to the prescribed diet. He has had a few minor respiratory infections without any serious complications and without any marked disturbance in his metabolism. His weight at the present time (May 20, 1937) is 39 pounds and his height is 39¼ inches. At present, he is receiving 6½ units of regular insulin in the morning and 7 units in the evening. Blood sugar determination (May 20, 1937) was 80 mg. Previous blood sugars had varied from 66 mg. to 105 mg. Occasionally, he has mild hypoglycemic reactions in the middle of the day following strenuous exercise, but these are readily controlled by orange juice and sugar.

In view of this boy's very satisfactory progress, would you advise changing him over to protamine zinc insulin and how and when would you do it?

D. S. G., male, born Jan. 2, 1936, and when first seen by us at the age of a few weeks, was entirely normal and remained so until November, 1936, when the mother began to notice that the child had excessive thirst with consequent polyuria. His weight on Nov. 14, 1936, was 21 pounds 5 ounces and, except for an acute cold, the physical examination was negative. However, a specimen of urine showed sugar 4-plus and acetone 3-plus, and the sugar was identified as glucose. Blood sugar, two days later, was 100 mg. Obviously we could not make a diagnosis of diabetes at this time but told the parents he should be treated as a potential diabetic. We did not have to wait long, because two days later he began to vomit and the following day became very drowsy and acidotic. Blood sugar on this date (Nov. 19, 1936) was 348 mg. He was accordingly hospitalized and his glucose tolerance determined. He was placed on an appropriate diabetic diet with 8 units of protamine zinc insulin before breakfast. We have followed him at intervals since this period and his weight has risen from 20 pounds 2 ounces (Nov. 19, 1936) to 29 pounds 5 ounces (May 28, 1937). His present height is 33 inches. During the month of February, 1937, he had an acute respiratory infection with suppurative otitis media, from which he made an uneventful recovery without any visible trace of acidosis. We have had gradually to increase the dose of insulin, however, from 8 units to 14. At the present time he is doing quite satisfactorily on a dosage of 12 units. Blood sugar determination (May 28, 1937) was 100 mg.

In view of the satisfactory progress of this boy so far, and in view of the very early onset of the disease, what would you say, in the light of your experience, as to the possibility of such a child's eventually being able to regain normal pancreatic function with discontinuance of insulin therapy?

CHAIRMAN JOSLIN.—I would recommend protamine insulin for these children. As reported in world literature about fifty children have developed diabetes under one year. Five children have developed diabetes under one year in our series—youngest seven months.

ALVAH L. NEWCOMB, Chicago.
HENRY H. PERLMAN, Philadelphia.
Secretaries.

SEVENTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

Round Table Discussion on Glomerulonephritis

Chairman: John D. Lyttle, M.D.
Assistants: Allan M. Butler, M.D.
Lee Farr, M.D.

CHAIRMAN LYTTLE.—In their studies of postscarlatinal nephritis, Escherich and Schick thought that the kidney had early in the course been sensitized in some way so that in the second or third week small amounts of pathogenic substance circulating would cause an injury while at any other time that amount would be tolerated without any reactions. This pathogenic material and the reaction called acute glomerulonephritis are believed to be connected in some way with antigen-antibody reactions known to be going on at this time. Shick noted the analogy between course of events in scarlet fever and the group of allergic reactions just being studied at that time. Since then a lot of kidney damage has been done to various animals, but the experimental studies have not been of great help to the clinician. Masugi in 1928 began his studies on nephrotoxins. This work seems important and I have asked Dr. Farr to discuss this type of experimental nephritis.

Experimental Nephritis

Dr. FARR.—The etiology of acute hemorrhagic nephritis is a most obscure subject. Clinical investigations have done little to shed any bright light on the cause of the disease, and experimental efforts have fared but little better. At Dr. Lyttle's request, today I shall not discuss the streptococcus etiology, the hypothesis of exposure to cold or the factor of heavy metal poisoning, but shall confine my remarks during the limited period to a discussion of a type of experimental nephritis with which we have recently been working and which may or may not be of value in explaining the phenomena seen in human nephritis.

The study of nephrotoxins (which term I shall use throughout as designating an antikidney serum) goes back to Lindemann in 1900. He injected guinea pigs with rabbit kidney and found that if he injected this resulting guinea pig sera into rabbits, albuminuria and cylindruria resulted. Pathologic sections of such kidneys showed tubular degeneration. Pearce in 1903 took up and extended Lindemann's observations. Although he was unable to produce an autonephrotoxin, he did show that many of the sera which had been called organ specific depended for their action on the presence of hemagglutinins and hemolysins. Pearce removed these factors by perfusing his organs before injection. Antikidney serum made with such an antigen induced cylindruria and albuminuria, whereas antisera prepared by immunizing with unperfused kidney induced an additional feature—hematuria. This antiserum, however, was only relatively organ specific: that is, it exerted its greatest effect upon the kidney but was not without simultaneous effect upon other organ systems. The experimental nephritis which Pearce produced was always of short duration, and the pathologic renal lesion consisted of tubular degeneration with occasional hyaline thrombi in glomerular capillaries. Woltmann and Sata in 1905 and 1906, respectively, repeated Pearce's work and came to the same conclusion regarding the relative specificity of nephrotoxin. Then for a period there was little or no work done with these agents until 1920, when Wilson and Oliver prepared an antikidney serum free of hemagglutinins and hemolysins which produced marked glomerular as well as tubular lesions. These authors considered nephrotoxin to be organ specific since absorption of the antiserum with kidney cells completely removed its nephrotoxic effect. Takeda in 1928 observed fibrin thrombosis and hemorrhage in the glomerular tufts of acutely affected animals as well as tubular degeneration, and he also noted an elevation of blood nitrogen values. Masugi, however, reawakened interest in this field with a series of papers beginning in 1928. He obtained the first convincing evidence of a chronic nephritis induced by the injection of nephrotoxin and made certain functional studies on rabbits in which he had produced this chronic disease. Fahr agreed with Masugi as to the similarity of the renal lesions which were obtained in this fashion to diffuse human glomerulonephritis. In 1935 Klinge and Klepper reopened the subject of autonephrotoxins which they claimed to be able to produce by injecting kidney emulsion and swine serum. Fahr examined sections of the kidneys of these animals and came to the decision that the lesions so induced were different from those obtained by Masugi.

At about this time Dr. Smadel, working with Dr. Swift on a general study of cytotoxic sera, took up studies on nephrotoxin as being very suitable for observation of cytotoxic phenomena. Since this gave us at the same time an opportunity to observe an experimental nephritis, we began a collaborative effort.

The antisera were produced by injecting rabbits intraperitoneally with 10 c.c. of a 10 per cent or 20 per cent suspension of perfused rat kidney. Injections were made on three consecutive days each week for a period of three weeks. Ten days after the last injection, test bleedings were made. This procedure was repeated three times over a period of three months, when the sera were finally taken for use.

It was not possible to determine the nephrotoxic power of the sera by titrating the antibody in vitro. Sera which showed a high precipitin titer might be low in nephrotoxic power, so biological assay was reported too. The good sera were then retained for use.

The nephrotoxic factor in serum is in the globulin fraction. It is not removed by absorption with red cells or serum, is completely removed by absorption with kidney, and is markedly decreased by absorption with liver. The serum is species specific and rat serum had no effect in mice or guinea pigs.

Nephritis was produced in rats by injecting on the average 0.3 to 0.4 c.c. of a good nephrotoxic serum per 100 gm. of animal weight. The same strain of rat was used for this experiment as was used for the serum production. Usually the serum was given in divided doses since in this manner anaphylactoid reactions were avoided while nephrotoxic effect was in no wise lost. The serum was injected intravenously diluted with fresh Ringer's solution.

Before this was done each rat was observed for a control period of about one month when urea clearances, plasma protein and hemoglobin determinations, and urinalyses were done to rule out any preexisting renal lesion. If all these tests fell within the normal range, the animal was used.

Within a few hours after injection of the nephrotoxic sera the animals developed a very severe proteinuria, usually losing protein in the urine in a concentration approximating 40 gm. per liter. During the first few hours when this proteinuria was excessive, the animals for the most part had from moderate to severe oliguria. Urine flow reestablished itself within twenty-four hours as a general rule. The albuminuria, however, persisted in a marked degree for the duration of the disease. Casts were first noted in the urine about the second day of the disease and remained in large numbers until the animal died or made a recovery. About the third day of the induced disease marked subcutaneous edema and ascites were present. At this time the animals presented a nephrotic picture in many respects. There was no hypertension; the blood proteins were markedly reduced; there were massive edema and ascites, the added fluid often amounting to 30 per cent of the animal's weight.

There is marked lipemia and a complete absence of hemorrhagic phenomena. This edematous phase usually clears up in a few days, but may persist as long as three weeks. During this period there is no demonstrable reduction in ability of the kidney to excrete urea as measured by the urea clearance test, and there is no anemia. Their appetites are good, and they are far from feeling as ill as they appear. With disappearance of the edema the plasma proteins show a rise to near normal levels, but the albuminuria and cylindruria are not abated. For the next month there is very little change in the animal, following which period a gradual reduction in renal function, as measured by the urea clearance test, becomes manifest. When the kidneys are so damaged that the urea-excreting power has been diminished by about 50 per cent, hypertension begins to become an important factor of the disease. After this time the disease marches on to a fatal termination, a progressive fall in the urea clearance, a sustained rise in the blood pressure, increasingly severe anemia, an increasing retention of nitrogen, and a growing plasma protein deficit. When the nephritis so induced is severe enough to cause death within six months, the animal generally ceases to grow within three weeks to a month after injection of the nephrotoxin. Terminally there is a sharp loss of weight, and marked malnutrition becomes increasingly evident, despite the fact that the animals eat their usual rations. We have not been able to demonstrate definite retinopathy in the terminal stages, although it is my impression there is arteriolar constriction but the vessels are exceedingly difficult to visualize because of the severe degree of anemia present. Examination of the bones histologically and calcium and phosphorus determinations

have revealed no abnormalities. Throughout the disease period the animals appear to be able to excrete sodium chloride without difficulty. Occasionally doubly refractile globules are seen in the urine.

Chemically and clinically these rats demonstrate a state which is similar in many respects to human Bright's disease following a streptococcal infection after the nephritis has become chronic.

If relatively large doses of nephrotoxin were injected at frequent intervals, a rapidly fatal nephritis was produced. By using smaller injections and not repeating them, the chronic disease was obtained. A certain number of animals made a complete recovery after exhibiting all of the signs of the disease.

Histologic and gross examination of the kidneys of animals so treated show a variety of pathologic lesions. When the animals are killed during the initial phases of the disease, the kidneys appear rather pale and edematous. Histologic examination revealed diffuse involvement; swelling of the intercapillary substance of the glomerular thickening of the basement membrane and tubular degeneration were prominent. Proliferative changes at this time were inconspicuous, and there was very slight cellular infiltration. The epithelial cells of the tubules were the seat of cloudy swelling and of hyaline droplet degeneration. Many of the tubules were markedly dilated. Collections of cells were frequently present about small vessels in the kidney. These appeared about the fourth day and increased thereafter. These microscopic lesions of the early phase merge into scarring of the glomeruli and tubules. Those examined later in the disease showed well-marked proliferative changes and glomerular crescents. This proliferation of the cells of Bowman's capsule is followed by connective tissue in growth and finally by complete replacement of the glomerulus by scar tissue. In animals with chronic progressive nephritis different individual glomeruli would often show these processes in all stages. The terminal result is a scarred somewhat shrunken kidney with little of its original architecture left intact and practically without functional value. The striking similarity of these kidneys to those which are seen as the end-result of postscarlatinal nephritis is of considerable interest. The fact that this process may under suitable conditions be arrested at any stage or may progress to destruction or recovery is food for thought. The difficulty of demonstrating the presence of these original nephrotoxins is emphasized by the fact that 9 c.c. of serum from a rat with this type of chronic nephritis has been given to a normal rat without effect. The nephrotoxin seems to act as an original noxious agent, which then disappears but which acts in such a fashion as to lay the foundations for a chronic progressive disease with the first blow. The factors operating here thereby causing the lesion to become chronic or to resolve may be in part at least similar to those operating in acute hemorrhagic nephritis.

DR. JOSEPH W. EPSTEIN (CLEVELAND, OHIO).—Your experiments with nephrotoxin indicate an attack on the tubules before the glomeruli are affected. Is this the same in human acute nephritis? Also the fact that there is very little nitrogenous retention with edema—would you say that you produced a nephrosis instead of a nephritis?

DR. FARR.—So far as we can determine, the nephrotoxin affects the glomeruli as well as the tubules. The glomerular changes are not so striking as the tubular changes, but they are definite and always present. The most consistent change is thickening of the basement membrane. In human acute nephritis we believe the glomeruli and tubules are also simultaneously affected, although the tubular changes are not as striking as in the nephrotoxic nephritis.

In regard to the question in which you ask whether we have produced a nephrosis instead of a nephritis since the animal showed an edema with little nitrogen retention, there is no evidence to show that we have actually produced a nephrosis since the animals developing the chronic disease usually died of renal failure; if you

like, you might call it a nephrotic stage, but I believe such artificial discrimination in such experimental disease confuses rather than clarifies.

DR. MYLNOR W. BEACH (CHARLESTON, S. C.).—Does the concentration in the tubule have any effect on the degree of pathology?

DR. FARR.—Your question whether the concentration of supposed excreted nephrotoxin in the tubules has any effect on the degree of pathology cannot be definitely answered. However, I may say that the evidence which we have obtained indicates that the renal injury is dependent solely upon the amount of nephrotoxin injected regardless of its administration, that is, whether it is given in single or divided doses, and from this we may infer that the concentration in the tubules is not the determining factor.

DR. DAVID GABERMAN (HARTFORD, CONN.).—How do you explain Aldrich's idea that the high protein diet results in improvement of his patient's nephritis and general condition?

DR. FARR.—Dr. Aldrich's experiences with high protein diets are consistent with our observations. We have merely determined the quantitative level for optimal assimilation. Patients fed more than this optimal diet do retain and assimilate protein but do not, in our opinion, do it in the most efficient manner. It is my impression of clinical observation also that children on high protein diets do well, but we believe they do better on the optimal protein diet as determined by our balance experiments.

DR. JONATHAN P. HADFIELD (FALL RIVER, MASS.).—What rôle does the creatine ratio play?

DR. FARR.—The creatine ratio or creatine clearance is of value in determining the extent of glomerular involvement. We have used the urea clearance in preference since it is easier to carry out on children, and we believe the results are more informative. However, we have done many creatine clearances and find that creatinine, inulin, and urea clearances all run parallel. We find the urea clearance to be of considerable aid in prognosis since the urea clearance returns to normal frequently months before there is any improvement in the concentrating ability of the kidney and before there is any significant change in the urinary sediment.

CHAIRMAN LYTTLE.—The classical case of acute hemorrhagic nephritis will not fail to be diagnosed. The onset following a streptococcal infection with hematuria, edema, and hypertension is so striking and alarming that the child is usually brought to a doctor. But a large number of cases of acute glomerulonephritis do not show edema or hypertension, and urinary abnormalities which are commonly overlooked may be the only sign of the disease. The nephritis runs a brief course and ends in complete cure without diagnosis or treatment. In discharging a patient with tonsillitis, the practitioner may get a report of urine which shows albuminuria, casts, and cells, and further observation will show that these findings persist for a short time and then disappear. The patient is entirely well, has no extrarenal symptoms, and has good kidney function. It is probably unwise to tell parents that the child with traces of albumin, a few casts, and cells in the urine has Bright's disease. But I think that, even though the disease is mild and transient, the clinician who observes these subclinical changes following a streptococcus infection should bear in mind their prognostic significance and should realize the importance of careful follow-up observations.

Differential Diagnosis.—The following conditions must be considered: (1) Nephrosis, (2) benign albuminuria with minimal microscopic findings (orthostatic albuminuria, etc.), (3) acute exacerbation of chronic nephritis, and (4) embolic nephritis—subacute bacterial endocarditis.

1. The differential diagnosis between nephrosis and acute glomerulonephritis should offer no difficulty. Its chief importance is in prognosis. Acute nephritis follows a hemolytic streptococcus infection, and significant hematuria is always present at onset. Edema and hypertension may or may not be present. The edema of nephritis, in contrast to that of nephrosis, is rarely generalized or as massive. Nephrosis may develop following an infection, but the infection is usually a mild upper respiratory involvement, and the hemolytic streptococcus is rarely found. Clinically the important points in favor of nephrosis are generalized edema with apparent well-being and normal blood pressure: from the laboratory, reports are obtained of heavy persistent albuminuria without significant hematuria, no nitrogen retention in the blood, low serum albumin, and high blood cholesterol. Here I should like to point out that at the onset in acute glomerulonephritis we may find moderately low serum protein and high serum cholesterol. This does not necessarily mean a nephritic element in the nephritis. The low serum protein can occur before albuminuria has been present long enough to deplete serum protein. It is possible that these changes in blood chemistry are related to the infection which has set up the nephritis.

2. *Benign Albuminuria (Including Physiologic, Orthostatic, Malnutrition).*—Albuminuria without striking changes on physical examination and without well-marked microscopic findings (cylindruria and hematuria) is commonly seen in young children and during puberty. If the urine is examined repeatedly, the incidence is from 12 per cent to 68 per cent of all children. It is more common in girls. In the majority of the cases serum albumin is the protein identified, but in a number of cases, in addition to albumin, a substance precipitated by acetic acid in the cold is found. A careful examination of the sediment will sometimes show a few hyaline and granular casts and a few red cells. This does not necessarily mean that nephritis is present, for it is entirely possible that the same mechanism which allows protein to leak through the kidney will also allow a few red cells and casts to pass.

Attempts have been made to classify these albuminurias on the basis of some outstanding clinical feature which may accompany the case. It would seem that there are many factors which can be responsible for the condition, but until we know more about the etiology and pathogenesis, we should not be too specific. Physiologic albuminuria is found in the newborn, after exercise, and exposure to cold. It does not persist when the cause is removed. When orthostatic albuminuria is present, the urine voided in the recumbent position contains no albumin or only traces, while the urine voided in the upright position contains variable amounts of albumin and usually a substance precipitated by acetic acid. A few red cells and casts may sometimes be found. This condition is commonly found in boys, from four to sixteen years of age, who are growing rapidly, have signs of vasomotor instability and usually poor posture with lordosis. Kidney function is normal, and serum proteins show no changes. The course is variable, but the condition usually disappears after puberty, and there is no evidence that it leads to nephritis in later life. In a group of children with faulty hygiene—anemia, malnutrition, and foci of infection—Calvin and coworkers found that 60 per cent showed albuminuria. In some children the albuminuria disappeared when the foci of infection were treated or removed. In a second group of children, well cared for and without foci of infection, 15 per cent showed albuminuria.

The chief problem is differential diagnosis. This is an important question and often a difficult one to settle. Even after long study one may not be satisfied that the diagnosis is correct. If one finds repeatedly and without difficulty a number of red blood cells and casts, especially red blood cell casts, the diagnosis is probably mild glomerulonephritis even though there are no extrarenal symptoms and kidney function is normal. We have found the Addis sediment count of great help in differential diagnosis. By this method the number of cells and casts excreted in a period of time is measured and compared with the findings in normal children. If the Addis

count repeatedly shows a definite increase in excretion of erythrocytes, leucocytes, epithelial cells and casts, especially the red blood cell casts, the diagnosis is probably glomerulonephritis. If we can elicit a history of streptococcal infection preceding the urinary changes, this is a point in favor of the diagnosis of nephritis but does not prove it. It should be borne in mind that orthostatic albuminuria may follow postscarlatinal nephritis and also that the erect position may increase the albuminuria in nephritis. The burden of proof is on the physician who diagnoses benign albuminuria. Careful and long-continued observation may eventually clear up the diagnosis. Except for general indications revealed by history and physical examination, no treatment is necessary in benign albuminuria.

There are other conditions not primarily related to the kidney in which albuminuria with microscopic hematuria and cylindruria occurs. In acute infections and in diseases such as intestinal intoxication and high intestinal obstruction and vomiting where dehydration is an important part of the picture, variable degrees of albuminuria, usually with microscopic changes (casts and cells), are observed. This is also true in severe ketosis in children whether the ketosis results from diabetes mellitus, starvation, periodic vomiting, or a ketogenic diet. A well-marked albuminuria with cylindruria is found during the crises of paroxysmal hemoglobinuria. In the case of galactosuria reported by Mason, a heavy albuminuria with cylindruria and microscopic hematuria was observed when the child was on a milk diet, while on a milk-free dict the urine was normal. In acute rheumatic carditis, with or without cardiac failure, jaundice, passive congestion, albuminuria with casts and red blood cells in the sediment are commonly observed. In cerebral conditions such as subdural hematoma, convulsions, and pituitary tumors albuminuria is common.

DR. F. H. ALLEN (HOLYOKE, MASS.).—Are there any statistics to show any increased liability to nephritis in patients with orthostatic albuminuria followed for fifteen or twenty years? Also are such persons accepted as good risks by insurance companies?

CHAIRMAN LYTTLE.—All studies that I am familiar with show no increased liability to nephritis in patients with orthostatic albuminuria. I do not know what attitude insurance companies take.

DR. HADFIELD.—Do you treat all these cases with minimal nephritis findings as potential cases of nephritis?

CHAIRMAN LYTTLE.—The only treatment called for in children with minimal urinary findings is continued observation until the urine is normal.

3. In older children the question frequently arises as to whether we are dealing with an acute glomerular nephritis or an *acute exacerbation of chronic nephritis.* Urinalyses prior to the onset of the symptoms would be of utmost help in the attempt to answer this question. As the differential diagnosis is important in prognosis, the history must be carefully examined in order to answer the question. In chronic glomerulonephritis a story of long-continued ill health with malnutrition, anemia, dyspnea, and fatigue may be elicited. There may be chronic upper respiratory infection, urinary tract signs such as frequency or polyuria, and there may be an episode which, in retrospect, can be translated into the initial attack of acute glomerulonephritis. On physical examination the signs of advanced kidney disease such as well-marked and persistent hypertension with cardiac enlargement, palpable peripheral vessels, and changes in the fundi indicate chronic nephritis. The high blood pressure and enlarged heart, which may occur in acute glomerular nephritis, do not persist after recovery. It is a very difficult problem, and hence the clinician is frequently mistaken in his initial impressions.

4. In *subacute bacterial endocarditis* we may see variable urinary changes which indicate renal damage. There is no way of telling certainly whether we are dealing

with multiple emboli, infarction, or ordinary glomerular nephritis. Good kidney function and the absence of extrarenal signs are not necessarily significant. A benign form of hemorrhagic Bright's disease has been described, which is said to be due to focal nonembolic nephritis. This is an anatomic diagnosis; I know of no way of making this diagnosis clinically.

In the diagnosis of chronic glomerulonephritis the chief difficulty is in differentiating nephrosis from the nephrotic stage of chronic glomerulonephritis. An accurate history and complete laboratory data at the onset of the disease are helpful. Even when most of the findings suggest nephrosis, if the onset has followed an infection with hemolytic streptococcus and was characterized by hematuria and hypertension, the diagnosis of nephrosis is excluded. But glomerulonephritis may resemble nephrosis very closely in its onset and course, and diagnosis will remain in doubt unless retinitis, severe hypertension, or impaired renal function occurs. Aldrich discards the diagnosis of nephrosis if hypertension is present or if red blood cells are found in the urine. From our own experience and from the literature it seems well established that many children with anatomically proved nephrosis show moderate hypertension and microscopic or even gross hematuria. The significance of this hematuria and hypertension is not known; it does not necessarily mean that the patient has chronic glomerulonephritis. It may, however, signify renal irritation or a mild form of acute glomerulonephritis which can go to complete recovery. The following case is cited as an instance of this:

The patient under close observation showed only nephrotic signs and symptoms in the first five months of the disease. Following streptococcus infection an acute glomerulonephritis (i.e., hematuria, hypertension) developed, lasted three months, and eventuated in complete clinical recovery. The signs of nephrosis persisted. Autopsy seven months after the attack of acute glomerulonephritis showed no lesions in the glomeruli.

When severe hematuria and hypertension develop and persist in a child whose course from the onset has been typical of nephrosis and in whom renal failure eventually supervenes, it is usually assumed that the diagnosis at the onset was incorrect. The majority of children with acute glomerulonephritis recover without developing chronic glomerulonephritis, and the same is true of nephrotic children who develop acute glomerulonephritis. Although it is uncommon for a patient with true nephrosis to develop acute and subsequently chronic glomerulonephritis and renal failure, it sometimes occurs.

In spite of the difficulties which often attend diagnosis, there can be no doubt that nephrosis is a distinct entity; it is clear, however, that signs of nephrosis and of glomerulonephritis frequently occur together in the same patient. When at its onset the disease picture is that of glomerulonephritis, and signs of nephrosis subsequently make their appearance, these signs may be taken to indicate the chronic nature of the original process; the outcome is usually fatal. In such cases the major disease is chronic glomerulonephritis and to them the term nephrosis should not be applied. However, when glomerulonephritis supervenes in the course of nephrosis, it is often an acute process which differs from the disease in uncomplicated form only by a somewhat longer course. It need not necessarily influence the favorable outcome of the nephrosis. In the interest of prognosis, then, the attempt to differentiate between these two processes is eminently justified. Of eight of our cases of nephrosis in which the diagnosis was confirmed at autopsy, hematuria occurred in five and hypertension in six. In addition to the pathologic data, the clinical course in these cases was typical. In nephrosis complete recovery is common after long periods of edema and albuminuria; it is extremely rare in true chronic glomerulonephritis. Severe hypertension, cardiac hypertrophy and renal failure never occur in uncomplicated nephrosis and the almost specific susceptibility to pneumococcus infection is peculiar to nephrosis.

DR. H. G. PONCHER (EVANSTON, ILL.).—If the burden of proof is on the man to prove that a benign albuminuria is not a mild nephritis, is it not reasonable to also say that the burden of proof is on one who finds red blood cells and slight nitrogen retention in a patient with a picture of nephrosis to prove that this is not a mild nephritis? The fact that a patient showing these findings may die of pneumococcic peritonitis and show only minimal glomerular changes and major tubular pathology does not seem to be an adequate criterion for not classifying such a case as a nephritis. May not proved cases of nephritis show exactly such a picture?

CHAIRMAN LYTTLE.—If a patient, onset and course of whose illness have been typical of nephrosis, develops hematuria and hypertension, I suppose one must make a clinical diagnosis of mixed nephritis. Nitrogen retention in nephrosis is not a reliable indication of glomerular involvement. But our experence in the autopsy room, and I think Dr. Butler will agree with me in this, has shown that these patients do not have anatomic nephritis in spite of the presence of hematuria and hypertension. The cause of the hematuria and hypertension in true nephrosis is not known; it may be due to an acute nephritis which can heal quickly. I think we must rely on the anatomic findings as a final criterion of diagnosis, and acute nephritis does not give the anatomic picture we see in nephrosis.

Treatment of Acute and Chronic Hemorrhagic Nephritis

DR. BUTLER.—The mortality in the acute attack of hemorrhagic nephritis is usually considered to be about 5 per cent. Most pediatricians have felt that another 5 per cent of the cases progress from an acute hemorrhagic nephritis to a chronic progressive type of the disease. Very recently, however, Snoke has reported a follow-up study of 150 cases of hemorrhagic nephritis in children in which he has determined the presence or absence of a renal lesion by the Addis sediment count. From this data he concluded that the nephritis had completely healed in 40 per cent of the cases, had remained active nephritis in 40 per cent, and had proved fatal in 20 per cent. It is quite clear that if these figures are substantiated by further study the generally accepted prognosis in this disease must be altered.

CHAIRMAN LYTTLE.—More recently Dr. Snoke has made a similar follow-up study in Rochester, N. Y. The data on this series do not support the serious prognosis suggested by his San Francisco study.

DR. BUTLER.—Death occurs during acute hemorrhagic nephritis as the result of acute cerebral edema, congestive heart failure, infection, or a rapid progression of the nephritis and a true uremia. The bulk of evidence concerning the etiology and clinical course of the disease indicates that it is closely related to an infection, usually an upper respiratory one, and that a persistence of such an infection tends to prolong or aggravate the nephritis. Obviously, therefore, treatment must include the treatment of any focus of infection which may be related to the attack, in the hope that the severity of the disease will be shortened and recurrence prevented. Usually the related infection has subsided to such an extent by the time the nephritis has appeared that its treatment can be postponed until after the more acute manifestations of the disease have passed. Not infrequently, however, a peritonsillar or retropharyngeal abscess or a mastoiditis may demand immediate operation in spite of the presence of cerebral edema, hypertension, and myocarditis.

CHAIRMAN LYTTLE.—Do you think major surgery should be done in acute nephritis?

DR. BUTLER.—Obviously acute nephritis with cerebral edema, hypertension, and myocarditis does not provide the most opportune moment for major surgery. But operations such as an acute appendix must be done if the ordinary indications for operation are present.

DR. HORACE FRENCH (LANSING, MICH.).—Is there any choice of anesthesias for surgery during the acute or convalescent stage?

DR. BUTLER.—Aside from the indications of a particular operation, anesthesia should be considered as it would be for any patient with a severe myocarditis or cerebral edema.

Bearing in mind that the source of infection must be dealt with at the appropriate time, the immediate treatment is directed toward the cerebral edema, the hypertension, and the myocarditis.

Fortunately the imminence of the appearance of untoward symptoms and their course are readily detected by the degree of the oliguria, the course of the blood pressure, symptoms of increased intracranial pressure such as headache, nausea, and vomiting, the character of the pulse, size of the heart, pulse pressure, and obvious signs of decompensation. Thus untoward signs can be readily detected by the simplest type of clinical observation. It is our conception that the oliguria, hypertension, increased intracranial pressure, and congestive heart failure occur concomitantly and from a common cause—namely, a rather generalized arteriolar spasm which may be the result of a toxin, a nephrotoxin, or some allergic reaction. At least in the absence of any better concept this is a convenient one, for it gives a simple explanation for the effectiveness of the magnesium sulfate therapy which Blackfan and his coworkers have shown to be almost specific. Experimental work recently done by Ruben and Rapoport has shown that the inclusion of magnesium sulfate in the diets of rats inhibits the vascular spasm produced by ergotamine tartrate in rats not so protected. Such a vascular action seems far more likely than an osmotic action, for it is highly doubtful whether such small amounts of magnesium sulfate as are used intramuscularly would result in withdrawing fluid from the edematous brain to the blood stream. Whatever the explanation, magnesium sulfate empirically does lower the blood pressure, relieve the intracranial pressure, and increase the urine volume. Any direct effect that it has upon the heart is less obvious. If the cardiac symptoms are the result of spasm of cardiac vessels, the magnesium sulfate should be as specific for this manifestation of the disease as for the others. On the other hand, the cardiac picture is very similar to that produced by a toxic myocarditis. For this reason intravenous 25 per cent glucose and morphine may be given as therapy for the cardiac failure. There would seem to be some doubt as to whether digitalis should or should not be used. We have not used it extensively enough at the Children's Hospital to draw any conclusions. Dr. Stokes, of Philadelphia, believes it is beneficial. Because magnesium sulfate therapy is so specific, a rather detailed description of the manner of administering it seems justified.

From 4 to 8 c.c. of a 25 per cent solution of $MgSO_4 \cdot H_2O$ are given intramuscularly to any child whose systolic blood pressure is over 115, or whose blood pressure is observed to be rising, or who presents any significant symptoms of cerebral edema. If the blood pressure has not fallen at the end of two hours or if the blood pressure at a later period begins to rise, the dose is repeated. Concomitantly with parenteral injection, magnesium sulfate is started orally, from 1 to 2 ounces of a 50 per cent solution being given every four hours until the blood pressure has remained normal for twenty-four hours or until catharsis results. Though the magnesium sulfate therapy is accompanied by a loss of weight which runs parallel to the subsidence of symptoms, it is not given primarily as a cathartic but rather as a diuretic. Indeed, experience shows that the oral administration may be repeated every four hours for several days with little or no cathartic effect. Since substituting ten years ago the intramuscular for the intravenous administration of the magnesium

sulfate, we have encountered no case in which intravenous injection was required. All the patients entering the hospital with hypertension and nephritis whose blood pressures have not been lowered by intramuscular magnesium sulfate have been shown to have chronic nephritis or pyelonephritis. Since in such patients magnesium sulfate is ineffective and probably contraindicated, the differential diagnosis between an acute hemorrhagic nephritis and a chronic nephritis should be made before magnesium sulfate therapy is pushed.

In cases in which the oliguria is marked but the blood pressure is only slightly elevated, magnesium sulfate may be started by mouth more or less as a prophylactic measure, but we do not so prescribe it in every case of hemorrhagic nephritis.

DR. MARTIN MALINER (BROOKLYN, N. Y.).—Do you always have a hypertension? What do you call a hypertension? It seems to me you frequently see acute nephritis without a real hypertension.

DR. BUTLER.—Fortunately there is no doubt that such cases occur. In a child under twelve years of age a systolic pressure above 115 and a diastolic pressure above 80 indicates hypertension.

DR. GABERMAN.—Dr. Butler has discussed the treatment of the severe type of acute nephritis usually seen in the hospital, but how about the very early treatment of acute nephritis before the symptoms of headache, hypertension, myocarditis, develop as is seen in private practice?

DR. BUTLER.—General procedures will be mentioned in a moment. Reference to the mild case does bring up the question of the routine use of magnesium sulfate prophylactically. Dr. Lyttle, I believe, has an opinion about this that he might wish to express.

CHAIRMAN LYTTLE.—I believe Aldrich states that magnesium sulfate given routinely in all cases will prevent the development of cerebral edema.

DR. BUTLER.—The prophylactic use of magnesium sulfate may be beneficial, but let us remember, particularly in hospital practice, that an order for 1-2 ounces of 50 per cent magnesium sulfate every four hours has been given and let us see to it that it is stopped at an early date and not continued needlessly.

While using magnesium sulfate medication in the acute or mild case, the patient should not be permitted to become dehydrated enough to inhibit a moderate urine volume. Indeed, one should strive for a rather large urine volume, for as soon as this is obtained, the symptoms subside. To this end fluids should be given in liberal amounts, not restricted. To be specific, a child of six years should have between 1,000 and 1,200 c.c. of fluid per day. Not very much need be said concerning the diet of these children. During the period of acute symptoms the patient will be more or less nauseated and will not want to eat. Sweetened fluid should be given in order to provide an adequate intake of fluid and calories in the form of carbohydrate. Since the edema is due to the oliguria, not to a specific salt retention, restriction of sodium chloride is not important and is cared for by the fact that most sweetened fluids contain little or no salt. As soon as the child feels like eating, he can be permitted to eat. For some days his appetite is such that there is little danger of overeating, and we see no need of restricting his diet except as any ordinary child's diet is restricted.

DR. J. W. BRITTON (ANNISTON, ALA.).—What amount of protein would you use in the diet of a child with acute nephritis?

DR. BUTLER.—The remarks just made pretty well cover that question. At a time when protein might be harmful, the patient will almost certainly not eat it. In

acute nephritis any significant elevation of nonprotein nitrogen or other evidence of severe retention will almost always subside by the time the child feels like eating much protein.

DR. R. M. POLLITZER (GREENVILLE, S. C.).—Please explain the mechanism of the edema in acute nephritis.

DR. BUTLER.—I do not know that I can. The edema of nephrosis and chronic nephritis is usually closely related to the level of the plasma proteins. But the edema in acute nephritis is not accompanied by a low plasma protein osmotic pressure. It is probably related to the effect of the vascular reaction to the toxin or allergic reaction that underlies the disease.

When the hypertension, myocarditis, and gross hematuria have subsided, foci of infection should be dealt with. Tonsils that appear infected on examination, that are associated with enlarged cervical glands, and the history of repeated pharyngeal infections should be removed. I wish I knew how a sinusitis should be treated but I do not. At the Children's Hospital all patients with an initial hemorrhagic nephritis are not subjected to tonsillectomy.

DR. L. M. EARLE (HOLLYWOOD, CALIF.).—Have you any experience in the use of sulfanilamide in the treatment of the underlying infection?

DR. BUTLER.—Not in acute hemorrhagic nephritis. Perhaps Dr. Lyttle has.

CHAIRMAN LYTTLE.—We have used it cautiously in a few cases. If kidney function is impaired, the level of sulfanilamide in the blood must be carefully watched.

DR. B. BENJAMIN (MONTREAL, CANADA).—About what percentage of children with nephritis under your care have not had a tonsillectomy?

DR. BUTLER.—Any answer I gave to that question would be merely a guess, as I have never reviewed cases with that thought in mind. Dr. Lyttle has rather strong convictions on this point and I am sure has quantitative information concerning his patients.

CHAIRMAN LYTTLE.—Tonsillectomy had been performed previous to the onset of nephritis in approximately one-third of our patients. One should never have strong convictions about any aspect of nephritis. However, my attitude on foci of infection in nephritis is somewhat as follows: We do not know which cases of acute nephritis will progress to chronic nephritis, and we are ignorant of the mechanisms of both acute and chronic nephritis. There is clinical evidence that infection in the convalescent period has an adverse effect on the nephritis, and some good observers believe that persistent infection is a factor in the development of chronic nephritis. When chronic nephritis has been established, any attack on foci of infection is useless. Therefore, I recommend tonsillectomy in the ordinary case as soon as improvement sets in and the pharynx is not acutely inflamed. And when the nephritis does not improve on a suitable regime or there is a recurrence of sore throat and adenitis, tonsillectomy is done as soon as the condition of the throat permits. The postoperative flare-up is mild and is not to be compared to the true exacerbation of nephritis that follows a recurrence of infection. I admit the benefits are not proved, but to say that this procedure is harmful is not a valid criticism in the light of my experience.

DR. BUTLER.—The length of the rest in bed should be determined as much by the history of myocarditis and the subsidence of cardiac signs as by the character of the urine sediment. A few red blood cells and a trace of albumin may persist in the urine for weeks or months and may be a relatively poor guide in determining the patient's activities. But a patient should not be allowed up and about while

the heart is still enlarged, the pulse rate elevated, the electrocardiogram abnormal, and erythrocyte sedimentation rate elevated. If these things are normal, I do not see why the patient should not be allowed to be up and about after a few weeks. But great care should be taken for many weeks to avoid exposure to cold or wet and fatigue. In general, the patient should be treated as a cardiac case, neglecting the diet as is done in such cases and judiciously neglecting the urine.

There are a few other points one might mention: first, someone may want to know whether prophylactic medication can prevent nephritis. My answer in the present state of our knowledge concerning etiology is no. Certainly there is no reason for placing the scarlet fever patient on a low protein diet. Likewise the use of antitoxin or convalescent scarlet fever serum probably accomplishes little good. I wonder if Dr. Lyttle agrees.

CHAIRMAN LYTTLE.—I am unable to convince myself that we have any means of preventing acute nephritis.

DR. P. S. RHOADS (EVANSTON, ILL.).—In British fever hospitals it is felt that alkalinization of the urine in the first three weeks of scarlet fever prevents nephritis. Do you think low salt diets are helpful?

DR. BUTLER.—We know of no reason why low salt diets should be helpful in the prevention of acute nephritis. Any such beneficial effect of alkalinization as you mention may be due to the fluid intake and urine volume coincident to alkalinization. It is hard to take alkaline salts without taking considerable fluid.

A second question that may be in your minds is, Can the oliguria be treated by the ordinary diuretics? Our experience indicates that the xanthine derivatives produce little effect. Our opinion is that mercurial diuretics are definitely contraindicated. Third, Is intravenous sucrose effective in relieving the cerebral edema and its symptoms? I cannot answer the question because we have not used it in our clinic as we were a little hesitant in the presence of the oliguria to administer it in large enough doses to be effective. Possibly the drug would not only relieve the cerebral edema but also would have a diuretic effect.

DR. EPSTEIN.—Would you comment on the use of a lumbar puncture in the treatment of the child with acute hemorrhagic nephritis who is in a state of convulsion? Would you do a lumbar puncture or is it contraindicated?

DR. BUTLER.—As demonstrated by Dr. Blackfan these patients may have such an increase in intracranial pressure as to produce a pressure cone. Lumbar puncture if done at all should therefore be done very carefully. Intravenous magnesium sulfate is a much safer and more effective means of treating the cerebral symptoms.

I should like to stress that the magnesium sulfate therapy which is so effective in checking a course of events which may be fatal in hemorrhagic nephritis is ineffective and contraindicated in chronic nephritis. We have no specific therapy for the chronic form of the disease. In chronic nephritis our efforts should be directed toward removing foci of infection and maintaining the patient in as good a nutritional state as possible. Years ago Addis learned that he could usually benefit the nephritic patient referred to him by other doctors because he could abolish the dietary restrictions that had been prescribed. On the other hand, he could usually do little for the patient who came direct to him on a normal dietary regime. Keutmann and McCann have observed no ill effects from high protein diets in patients with moderately severe chronic nephritis. Aldrich and Boyle believed that a group of patients cared for by them did better on a high protein diet than on a diet restricted in protein. They stressed the advisability of including adequate amounts of all the vitamins. As anemia is always present in these patients, a deficiency of iron in the diet should be guarded against. Because chronic nephritis is almost

always progressive and the severity of the condition is changing, it is not unnatural that a diet which is optimal for the patient at one time will not be so at another time. Therefore, the above statements about diet must not be considered to apply to all chronic nephritic children.

In the early or latent stage of chronic nephritis there is usually a nephrotic aspect to the disease, and edema may be the most incapacitating symptom. The edema consists of water, sodium, and chloride, and there is ample evidence that such edema may be limited by the ingestion of minimal amounts of sodium chloride. Low salt diets should therefore be prescribed during the nephrotic stage of the disease. In the absence of cardiac involvement such edema is roughly inversely proportional to the concentration of the serum proteins. It is for the purpose of increasing the serum protein concentration and making good the loss of protein which occurs in the urine that high protein diets are frequently prescribed at this time. One must not forget that there is a certain amount of evidence obtained from animal experiments indicating that a high protein diet may have a deleterious effect upon the kidney.

DR. PONCHER.—Do you seriously believe that the exceptionally high protein diets are of value in regenerating serum protein? Most children refuse a high protein diet but succeed in regenerating blood proteins anyway.

DR. BUTLER.—Dr. Farr can tell you of some interesting experiments concerning the effectiveness of diets varying in their protein content in maintaining a positive nitrogen balance and concerning the effect of high protein diets upon the course of nephritis in rats.

DR. FARR.—I do not believe that such exceptionally high protein diets are of value in regenerating protein. Our experimental work indicates that protein in the diet is not assimilated by young children when more than 3 gm. of protein per kilogram of ideal body weight is fed. Our evidence shows further that when this limit is exceeded, actually less protein is assimilated than on the 3 gm. per kilogram diet.

DR. BUTLER.—As the nephritis progresses, there is an increasing tendency for nitrogen and other retention. Though the urea clearance is increased by a protein diet, ample clinical evidence shows that in the later stages of the disease the protein content of the diet must be limited if significant retentions are to be avoided. Since the inability to excrete the end products of metabolism is the reflection of the kidney's inability to concentrate such substances in the urine, the urine volume should be large enough to provide maximum excretion of the substances that should be at low concentrations in the plasma. Papers by Holton and Rehberg and by Newberg and Lashmet and others have clearly proved these points.

Finally in the terminal stage of nephritis when the kidney function is down to 10 per cent of normal, there is an inability to conserve the substances that are of high concentration in the plasma just as there is an inability to excrete those substances that are present in the plasma in low concentration. As a result there is a tendency to excrete a large amount of water, sodium, and chloride. At this stage, therefore, the nephrotic tendency disappears unless cardiac failure complicates the picture. This inability to conserve sodium and chloride may be so marked that an increase in urine volume will not only cause an increase in the excretion of sodium and chloride but will actually result in an increase in the concentration of the sodium and chloride in the urine as the urine volume increases. Because it is essential that such patients have a large urine volume, good treatment coincidently causes the excretion of considerable sodium and chloride per day. We have found that a patient whose plasma sodium was reduced to 126 meq./l. and whose

plasma chloride was reduced to 88 meq./l. excreted 3-4 gm. of sodium chloride per day. It is, therefore, important that such patients be given an amount of sodium and chloride in the diet that will maintain for them a balance of these substances and water.

Thus it is clear that no single dietary regime can be followed in the treatment of a patient with chronic nephritis. The course of the disease must be followed accurately enough so that diets may be prescribed that will at all times provide as normal a physiologic state as is compatible with the changing renal function.

DR. BENJAMIN.—Have you observed nephrosis as a distinct entity which proceeded as such throughout the child's life?

DR. BUTLER.—We have had sixteen patients at the Children's Hospital in Boston who we believe had true lipoid nephrosis. Exactly eight of these have for years been well and apparently have completely recovered. Most of the others have been examined at necropsy. Though some had at some period moderate nitrogen retention and a fair proportion of red blood cells to white blood cells and cellular granular casts to hyaline casts and showed involvement of the glomerulae on microscopic study, they had cases of true nephrosis. In each such case the degree of the degenerative changes was such as to result inevitably in glomerular damage. Thus the nephritic part of the clinical and pathologic picture was due to the severity of the nephrosis.

ANNUAL MEETING OF REGION IV OF THE AMERICAN ACADEMY OF PEDIATRICS

The meeting was held on Nov. 4, 5, and 6, 1937, at the Ambassador Hotel, Los Angeles. Sixty-four members, 198 guests, and 46 exhibitors attended, according to the registration. There were 24 exhibition booths. The annual business meeting was held the evening of November 4 and the annual dinner, the following evening in the Cocoanut Grove. At the close of the sessions on November 6, the members attended the Stanford-University of Southern California football game.

Abstracts of the papers presented follow:

NOVEMBER 4

Recent Investigations With the Tuberculin Ointment Patch Test. Ernst Wolff, M.D., and S. Hurwitz, M.D., San Francisco.

Description of test made by applying a concentrated tuberculin ointment covered with adhesive plaster on arm was given. Control test was made on opposite arm. Positive reaction consists of papule and vesicle formation with redness. A total of 1,075 tests were made on 964 patients, aged three months to fifteen years. Agreement with Mantoux test in clinically active cases.

Advantages are ease of application, absence of pain, and stability of product.

Pyloric Stenosis. Harman Tremaine, M.D., Boise, Idaho.

General review of subject was given with author's method of treatment outlined. Hydration was accomplished by subcutaneous injection of fluid and intramuscular injection of blood. Usual Rammstedt operation used. Artificial feeding used postoperatively. In the discussion Dr. J. N. Nichols reported 287 cases at Children's Hospital, Los Angeles. Since 1930, 137 cases have been operated with five deaths, four of which were from complicating diseases.

A Case of Glycogen Storage Disease. Ezra Fish, M.D., Beverly Hills.

A case of von Gierke's disease in child aged two and one-half years, weighing 22 pounds, was reported. Abdomen was enlarged from birth. Liver was enlarged, extending below the umbilicus into pelvis; the edge was smooth and firm; the spleen was not felt. The fasting blood sugar ranged from 40 to 64 mg. per cent. Ossification centers showed development of six months. The blood cholesterol was 175 to 380 mg. The glucose tolerance curve rose slowly to 139 mg. in three hours and returned to normal in five hours. There was an absence of the usual hyperglycemic response to adrenalin. Extracts of whole pituitary gland failed to raise blood sugar, as did prolactin. A peritoneoscopic examination was done during life by Dr. John Ruddock, Los Angeles, who obtained a specimen for biopsy, which confirmed the diagnosis. Dr. Ruddock discussed the technique and advantages of this diagnostic method.

Calcium and Phosphorus Balance Studies in Children With Latent Hilar Glandular Tuberculosis. William A. Reilly, M.D., San Francisco.

Results: Tuberculous activity is accompanied by a negative calcium balance which could be converted into a positive calcium balance by giving calcium gluconate, 40 to 60 grains per day by mouth, but not by giving cod liver oil. The negative calcium balance diminished during convalescence. There was also a negative phosphorus balance during the active stages of tuberculosis, and cod liver oil diminished this loss.

A Case of Unusual Fungus Infection. Rieta Hough, M.D., San Diego. (By invitation.)

Report of case of *Penicillium glaucum* infection in a two-and-one-half-year-old girl, beginning in November, 1936, and ending in death April 25, 1937. The course was stormy with superimposed hemolytic streptococcus infection. Ethyl iodide inhalations produced temporary improvement.

NOVEMBER 5

Care of Skin of the Newborn: Prevention of Infection. L. Howard Smith, M.D., Portland.

Author's experience in treating 1,683 successive newborn babies by nonoiling and nonbathing is given. The vernix was not removed and skin not touched, except for the use of warm water on diaper region. Only two cases of suspicious pyodermia were observed. The advantages of the method are the lessened handling of the babies, the saving in nursing time, and the lessened incidence of skin infections. In the discussion Bonar advised the use of flexible collodion on the blebs. Grulee had applied the same treatment to premature infants with satisfactory results.

The Undescended Testicle. Norman Nixon, M.D., Los Angeles.

The author had treated 59 cases of true cryptorchidism in boys aged two and one-half to fourteen and one-half years. In one-third of the boys, descent of the testes resulted. Treatment consisted of 250 rat units intramuscularly three times a week for 30 injections. Then after a rest of three months a second course was given. In half of the cases acceleration of genital development was observed. In 17 of 37 failures, operation was done. Previous endocrine treatment made surgery easier.

The Present Status of Endocrinology as Related to Pediatrics. E. Kost Shelton, M.D., Los Angeles (By Invitation).

A review of endocrinology as related to pediatrics was given and will be published in full in JOURNAL OF PEDIATRICS.

Convalescent Serum, Its Uses and Preparation. C. M. Hyland, M.D., Los Angeles. (By invitation.)

1. Measles: 423 cases of contacts treated—72 per cent prevented; 25 per cent modified; 3 per cent given too late in exposure. 2,344 susceptible contacts collected from literature—67 per cent prevented; 28 per cent modified; 3.6 per cent developed measles with no deaths.
2. Scarlet fever: 242 contacts treated—96.6 per cent prevented; 2.4 per cent developed mild attenuated disease. One hundred cases of scarlet fever treated: 19 per cent developed complications, which is less than one-half of nontreated cases. Attenuation of disease noted in treated cases; also used in nonscarlet streptococcus infections.
3. Poliomyelitis: Speaker urged larger doses in treatment, according to the work of Levinson.

Growth and Development as Related to Pediatric Surgery. Herbert E. Coe, M.D., Seattle.

Various congenital defects may interfere with normal growth and development. Among these are syndactylism, congenital dislocation of hip, torticollis, hypospadias, congenitally deformed ears, harelip. Among acquired conditions are muscle transplantations, osteomyelitis, hemangiomas, and burn scars which may interfere with normal growth and development.

The Course of Asthmatic Children in the Southwest. Vivian Tappan, M.D., Tucson.

The results of transplanting asthmatic children to Arizona climate were favorable on the whole. The group with respiratory infections, chiefly sinusitis, and who were not highly allergic, did best. The results in the markedly sensitive children were not as good. Infections in sinuses and in the bronchial tract present in majority and these seemed benefited. The longer the stay, the more marked the improvement. After returning to home environment improvement was maintained in the majority after interval of six months to six years.

Results of Eight Years' Treatment of Epilepsy in Children. Howard Cooder, M.D., Los Angeles. (By invitation.)

Total cases received for treatment in eight years		412
Number of cases treated one year or more	169	
Cases with possible organic cause	25	
Cases without organic evidence (idiopathic)	144	

Length of time treated:		Time free of attacks at last visit:	
1 yr.	54 cases	1 yr.	48 cases
2 yr.	60 cases	2 yr.	27 cases
3 yr.	28 cases	3 yr.	3 cases
4 yr.	14 cases	4 yr.	4 cases
5 yr. and up	13 cases	5 yr. and up	1 case
	169 cases	Total free of attacks 1 yr. +	83 cases

Total stopped 1 yr. or more	83	48%
Total improved	53	31%
Total stationary condition	27	16%
Total worse	3	
Total died	3	5%
	169	100%
Relapsed after 1 yr. free	6 cases	

Kind of treatment and results:

	NO.		%
Diet only		23	
Diet cured	21		
Phenobarbital only		31	
Phenobarbital cured	24		
Diet and phenobarbital		115	
Diet and phenobarbital cured	38		
	83	169	48%
Boarding home	17 cases		

Some Observations on the Results of Direct Blood Transfusions. Alonzo Cass, M.D., Los Angeles (By invitation).

A study was made of 270 cases of direct blood transfusions in the Children's Hospital, Los Angeles. The majority were given in cases of pneumonia, blood dyscrasias, and gastrointestinal disturbances.

Conclusion: Transfusion may be a bone marrow depressant and is not unassociated with danger in pneumonia and in critically ill children.

Encephalography in Children. Harry Dietrich, M.D., Los Angeles (By invitation).

Indications and contraindications for use of encephalography were given with illustrative cases shown in x-rays.

NOVEMBER 6

Additional Uses for the Oxcillatocapacigraph. Barnet E. Bonar, M.D., and Con Fenning, M.D., Salt Lake City.

The instrument, which has been devised by Fenning to record graphically changes in volume or capacity of structures, was described briefly. Tracings were shown of the uterine activity and fetal activity, including fetal respiratory movements through the opened and unopened abdomens of experimental animals whose spinal cords had been transected. Records of cardiac movements of rat fetuses and turtles were shown as well as tetanic contractions of the skeletal muscles of the frog. The instrument has additional uses which can be applied to physiologic activity in humans, making it possible to record as many as four or five more-or-less synchronous movements at the same time with ease. Tracings were shown of Braxton Hicks contractions in the human, as well as respiratory activity, apex pulsation, neck pulsation and fontanel pulsation in a two-month-old infant. It is concluded that this instrument may be of value in making studies of human physiologic activity where ordinary methods now in use would be difficult or impractical.

Treatment of Adult Type of Pulmonary Tuberculosis in Childhood. Lloyd B. Dickey, M.D., San Francisco.

Notes on Therapy in Communicable Diseases. Paul M. Hamilton, M.D., Alhambra.

1. Diphtheritic myocarditis: Treatment consisted of parenteral injections of glucose with sufficient pitressin to hold systolic blood pressure near a low normal level. Importance of frequent blood pressure readings emphasized.
2. Scarlet fever: Dramatic improvement following use of convalescent human serum. Complication rate 9 per cent as compared with previous five-year rate of 35 per cent.

3. Typhoid fever: 95 cases treated with intravenous bacteriophage. This method is still under investigation and is not yet recommended for general use.
4. Tetanus: Use of large doses, usually 200,000 units recommended with but 6 deaths in 44 cases. These studies made at the contagious disease hospital, Los Angeles General Hospital.

Intestinal Allergy. Phillip E. Rothman, M.D., and Helen Hopkins, M.D., Los Angeles (By invitation).

Clinically, the cases fall into two general groups: the first is characterized chiefly by a persistent diarrhea, and the second by gastric retention. Associated with these disturbances are a failure to gain weight, increased susceptibility to respiratory infections, and an alteration in desposition. Eczema, asthma, hay fever, or urticaria is rarely present. The diarrhea with marked abdominal distention may closely simulate celiac disease. Intestinal parasites and a functional colitis should be excluded in the differential diagnosis. The second group with vomiting as a predominating symptom may be confused with a congenital organic intestinal obstruction. The authors have had excellent results with the elimination of those foods producing positive skin reactions and believe that they are justified in ascribing the disorder to an allergic etiology.

Wood Tick Paralysis in Children (Motion Picture Demonstration). E. J. Barnett, M.D., Spokane.

Picture taken from cases reported in the *Journal of the American Medical Association,* September 11, 1937.

Academy News

The following physicians have been elected to Fellowship in the Academy:

REGION I

John Giblin, New York, N. Y.
Julius Margolis, Coatesville, Pa.
Harold R. Mixsell, New York, N. Y.

REGION II

Hillard W. Willis, Coral Gables, Fla.

REGION III

James J. Donahue, E. St. Louis, Ill.
Harold O. Lund, Middletown, Ohio
John W. Maroney, Detroit, Mich.
Mark F. Osterlin, Traverse City, Mich.
Thomas P. Saltiel, Chicago, Ill.
Clara D. Tigay, Chicago, Ill.
Dwight A. Weir, Mansfield, Ohio.

Comments

THE decision of the executive committee of the Academy to change the 1939 annual meeting from the spring to the fall of that year, as reported in the minutes of their meeting in the JOURNAL last month (p. 131), is a wise change in our opinion. It implies a separation of the Academy meeting from that of the Section on Pediatrics of the American Medical Association. The American Medical Association has felt that the many meetings held in conjunction with their annual session has resulted in the many tails wagging the dog. On the other hand, many Academy members have felt that unless the two meetings were held close together, the attendance of pediatricians at the Section on Pediatrics would be cut down.

By changing the annual meeting to October, the Academy of Pediatrics falls in line with other large specialist groups as the College of Physicians and Academy of Otolaryngology. From the standpoint of being away from home and practice October is the best month for the pediatrician. The change further does away with the difficulty that has been encountered in securing suitable and adequate hotel facilities and with problems connected with the Academy exhibits.

THE Editorial Board of the JOURNAL feels it necessary once more to call attention to the problem of case reports submitted for publication. Only a limited number can be published in the JOURNAL; and hence many submitted must necessarily be returned to the authors. A case report to be accepted must contribute something to our knowledge of the condition described. Simple rarity or infrequency with which a condition has been described in literature only occasionally makes a case report worthy of permanent record in medical literature. It is not unusual for a case report to be submitted on the basis that the author has been able to find the condition reported but ten or twenty times in medical literature. Frequently to the knowledge of the Editorial Board many more cases have been seen and are in the records of our larger children's clinics, but have never been reported for the reason that nothing has been found in their study which has added to our previous knowledge of the condition.

While on this topic we might add that there is a tendency on the part of many authors to so overload a manuscript with unessential irrelevant details that the paper loses interest and force, and hence fails to register its points. We are certain that by careful rewriting many manuscripts submitted to the JOURNAL could be cut from two to three out of every ten pages, and thereby would gain both strength and clarity.